OIPE JC98 SEP 2 8 2004 PATENT & TRADEMARK OFFICE

```
      ATGTGGAAATGGATACTGACACATTGTGCCTCAGCCTTTCCCCACCTGCCCGGCTGCTGC
1     ---------+---------+---------+---------+---------+---------+    60
      TACACCTTTACCTATGACTGTGTAACACGGAGTCGGAAAGGGGTGGACGGGCCGACGACG

        M  W  K  W  I  L  T  H  C  A  S  A  F  P  H  L  P  G  C  C

      TGCTGCTGCTTTTTGTTGCTGTTCTTGGTGTCTTCCGTCCCTGTCACCTGCCAAGCCCTT
61    ---------+---------+---------+---------+---------+---------+   120
      ACGACGACGAAAAACAACGACAAGAACCACAGAAGGCAGGGACAGTGGACGGTTCGGGAA

        C  C  C  F  L  L  L  F  L  V  S  S  V  P  V  T  C  Q  A  L

      GGTCAGGACATGGTGTCACCAGAGGCCACCAACTCTTCTTCCTCCTCCTTCTCCTCTCCT
121   ---------+---------+---------+---------+---------+---------+   180
      CCAGTCCTGTACCACAGTGGTCTCCGGTGGTTGAGAAGAAGGAGGAGGAAGAGGAGAGGA

        G  Q  D  M  V  S  P  E  A  T  N  S  S  S  S  S  F  S  S  P

      TCCAGCGCGGGAAGGCATGTgCGGAGCTACAATCACCTTCAAGGAGATGTCCGCTGGAGA
181   ---------+---------+---------+---------+---------+---------+   240
      AGGTCGCGCCCTTCCGTACAcGCCTCGATGTTAGTGGAAGTTCCTCTACAGGCGACCTCT

        S  S  A  G  R  H  V  R  S  Y  N  H  L  Q  G  D  V  R  W  R
```

MATCH WITH FIG. 1B

FIG.1A

MATCH WITH FIG. 1A

```
     AAGCTATTCTCTTTCACCAAGTACTTTCTCAAGATTGAGAAGAACGGGAAGGTCAGCGGG
241  ---------+---------+---------+---------+---------+---------+  300
     TTCGATAAGAGAAAGTGGTTCATGAAAGAGTTCTAACTCTTCTTGCCCTTCCAGTCGCCC

      K  L  F  S  F  T  K  Y  F  L  K  I  E  K  N  G  K  V  S  G

     ACCAAGAAGGAGAACTGCCCGTACAGCATCCTGGAGATAACATCAGTAGAAATCGGAGTT
301  ---------+---------+---------+---------+---------+---------+  360
     TGGTTCTTCCTCTTGACGGGCATGTCGTAGGACCTCTATTGTAGTCATCTTTAGCCTCAA

      T  K  K  E  N  C  P  Y  S  I  L  E  I  T  S  V  E  I  G  V

     GTTGCCGTCAAAGCCATTAACAGCAACTATTACTTAGCCATGAACAAGAAGGGGAAACTC
361  ---------+---------+---------+---------+---------+---------+  420
     CAACGGCAGTTTCGGTAATTGTCGTTGATAATGAATCGGTACTTGTTCTTCCCCTTTGAG

      V  A  V  K  A  I  N  S  N  Y  Y  L  A  M  N  K  K  G  K  L

     TATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGA
421  ---------+---------+---------+---------+---------+---------+  480
     ATACCGAGTTTTCTTAAATTGTTACTGACATTCGACTTCCTCTCCTATCTCCTTTTACCT

      Y  G  S  K  E  F  N  N  D  C  K  L  K  E  R  I  E  E  N  G
```

MATCH WITH FIG. 1C

FIG.1B

MATCH WITH FIG. 1B

```
     TACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGGCAAATGTATGTGGCATTG
481  ---------+---------+---------+---------+---------+---------+  540
     ATGTTATGGATACGTAGTAAATTGACCGTCGTATTACCCTCCGTTTACATACACCGTAAC

      Y  N  T  Y  A  S  F  N  W  Q  H  N  G  R  Q  M  Y  V  A  L

     AATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGGAAAAACACCTCTGCTCAC
541  ---------+---------+---------+---------+---------+---------+  600
     TTACCTTTTCCTCGAGGTTCCTCTCCTGTCTTTTGTGCTTCCTTTTTGTGGAGACGAGTG

      N  G  K  G  A  P  R  R  G  Q  K  T  R  R  K  N  T  S  A  H

     TTTCTTCCAATGGTGGTACACTCATAG
601  ---------+---------+-------  627
     AAAGAAGGTTACCACCATGTGAGTATC

      F  L  P  M  V  V  H  S  *
```

FIG.1C

```
          1                                                                50
FGF4      MS.GPGTAAV ALLPAVLLAL LA........ .PWAGRGGAA APTAPNGTLE
FGF6      MSRGAGRLQG TLWALVFLGI LV........ .GMVVPSPAG TR.ANNTLLD
FGF5      .......MSL SFLLLLFFSH LILSAWAHGE KRLAPKGQPG PAATDRNPIG
FGF1      .......... .......... .......... .......... ..........
FGF2      .......... .......... .......... .......... ..........
FGF9      .......... .......... .......... ..MAPLGEVG NYFGVQDAVP
FGF7      .......... ......MHKW ILTWILPTLL .....YRSCF HIICLVGTIS
KGF2      .......... ......MWKW ILTHCASAFP HLPGCCCCCF LLLFLVSSVP
FGF3      .......... .......... .......... ........MGL IWLLLLSLLE
FGF8      MGSPRSALSC LLLHLLVLCL QAQVRSAAQK RGPGAGNPAD TLGQGHEDRP

          51                                                               100
FGF4      AELERRWESL VALSLARLPV AA..QPKEAA VQSGAGDY.. ...LLGIKRL
FGF6      S...RGWGTL LSRSRAGLAG EI......AG VNWESG.Y.. ...LVGIKRQ
FGF5      SSSRQSSSSA MSSSSASSSP AASLGSQGSG LEQSSFQW.. ...SPSGRRT
FGF1      ......MAEG EITTFTALTE KFN...LPPG .......N.. ...YK...KP
FGF2      ......MAAG SITTLPALPE DGGSGAFPPG .......H.. ...FK...DP
FGF9      FGNVPVLPVD SPVLLSDHLG QSEAGGLPRG PAVTDLDH.. ...LKGILRR
FGF7      LACNDMTPEQ M...ATNVNC ......SSPE RHTRSYDY.. ...MEGGDIR
KGF2      VTCQALGQDM VSPEATNSSS SSFSSPSSAG RHVRSYNH.. ...LQ.GDVR
FGF3      PGWPAAGPGA .......... ...RLRRDAG GRGGVYEH.. ...L.GGAPR
FGF8      FGQRSRAGKN FTNPAPNYPE EGSKEQRDSV LPKVTQRHVR EQSLVTDQLS
```

MATCH WITH FIG. 2B

FIG. 2A

MATCH WITH FIG. 2A

	101				150
FGF4	RRL.....YC	NVGIGFHLQA	LPDGRIGGAH	ADT.RDSLLE	LSPVERGV.V
FGF6	RRL.....YC	NVGIGFHLQV	LPDGRISGTH	EEN.PYSLLE	ISTVERGV.V
FGF5	GSL.....YC	RVGIGFHLQI	YPDGKVNGSH	EAN.MLSVLE	IFAVSQGI.V
FGF1	KLL.....YC	SNG.GHFLRI	LPDGTVDGTR	DRSDQHIQLQ	LSAESVGE.V
FGF2	KRL.....YC	KNG.GFFLRI	HPDGRVDGVR	EKSDPHIKLQ	LQAEERGV.V
FGF9	RQL.....YC	R.T.GFHLEI	FPNGTIQGTR	KDHSRFGILE	FISIAVGL.V
FGF7	VRR.....LF	CRT.QWYLRI	DKRGKVKGTQ	EMKNNYNIME	IRTVAVGI.V
KGF2	*WRK.....LF*	*SFT.KYFLKI*	*EKNGKVSGTK*	*KENCPYSILE*	*ITSVEIGV.V*
FGF3	RRK.....LY	CAT.KYHLQL	HPSGRVNGSL	.ENSAYSILE	ITAVEVGI.V
FGF8	RRLIRTYQLY	SRTSGKHVQV	LANKRINAMA	EDGDPFAKLI	VETDTFGSRV

	151				200
FGF4	SIFGVASRFF	VAMSSKGKLY	G.SPFFTDEC	TFKEILLPNN	YNAYESYKYP
FGF6	SLFGVRSALF	VAMNSKGRLY	A.TPSFQEEC	KFRETLLPNN	YNAYESDLYQ
FGF5	GIRGVFSNKF	LAMSKKGKLH	A.SAKFTDDC	KFRERFQENS	YNTYASAIHR
FGF1	YIKSTETGQY	LAMDTDGLLY	G.SQTPNEEC	LFLERLEENH	YNTYISKKH.
FGF2	SIKGVCANRY	LAMKEDGRLL	A.SKCVTDEC	FFFERLESNN	YNTYRSRKY.
FGF9	SIRGVDSGLY	LGMNEKGELY	G.SEKLTQEC	VFREQFEENW	YNTYSSNLYK
FGF7	AIKGVESEFY	LAMNKEGKLY	A.KKECNEDC	NFKELILENH	YNTYAS....
KGF2	*AVKAINSNYY*	*LAMNKKGKLY*	*G.SKEFNNDC*	*KLKERIEENG*	*YNTYAS....*
FGF3	AIRGLFSGRY	LAMNKRGRLY	A.SEHYSAEC	EFVERIHELG	YNTYASRLYR
FGF8	RVRGAETGLY	ICMNKKGKLI	AKSNGKGKDC	VFTEIVLENN	YTALQNAKY.

MATCH WITH FIG. 2C

FIG. 2B

MATCH WITH FIG. 2B

	201				250
FGF4	.....	GM.....FI	ALSKNGKTKK	G..NRVSPTM	KVTHFLPRL.
FGF6	.....	GT.....YI	ALSKYGRVKR	G..SKVSPIM	TVTHFLPRI.
FGF5	.....	TEKTGREWYV	ALNKRGKAKR	GCSPRVKPQH	ISTHFLPRFK
FGF1	.....	...AEKNWFV	GLKKNGSCKR	G..PRTHYGQ	KAILFLPLPV
FGF2	.....	...T..SWYV	ALKRTGQYKL	G..SKTGPGQ	KAILFLPMSA
FGF9	HV.....	..DTGRRYYV	ALNKDGTPRE	G..TRTKRHQ	KFTHFLPRPV
FGF7	.....AKW	THNGGEM.FV	ALNQKGIPVR	G..KKTKKEQ	KTAHFLPMAI
KGF2	*.....FNW*	*QHNGRQM.YV*	*ALNGKGAPRR*	*G..QKTRRKN*	*TSAHFLPMVV*
FGF3	TVSSTPGARR	QPSAERLWYV	SVNGKGRPRR	G..FKTRRTQ	KSSLFLPRVL
FGF8	.....	.....EGWYM	AFTRKGRPRK	G..SKTRQHQ	REVHFMKRLP

	251				300
FGF4	.....	.....	.....	.....	.....
FGF6	.....	.....	.....	.....	.....
FGF5	QSEQPELSFT	VTVPEKKNPP	SPIKSKIPLS	APRKNTNSVK	YRLKFRFG..
FGF1	SSD.....	.....	.....	.....	.....
FGF2	KS.....	.....	.....	.....	.....
FGF9	DPDKVPELYK	DILSQS....	.....	.....	.....
FGF7	T.....	.....	.....	.....	.....
KGF2	*HS*.....	.....	.....	.....	.....
FGF3	DHRDHEMVRQ	LQSGLPRPPG	KGVQPRRRRQ	KQSPDNLEPS	HVQASRLGSQ
FGF8	RGHHTTEQSL	RFEFLNYPPF	TRSLRGSQRT	WAPEPR....	.....

MATCH WITH FIG. 2D

FIG.2C

MATCH WITH FIG. 2C

	301
FGF4	.....
FGF6	.....
FGF5	.....
FGF1	.....
FGF2	.....
FGF9	.....
FGF7	.....
KGF2	.....
FGF3	LEASAH
FGF8	.....

FIG.2D

```
GGAATTCCGG GAAGAGAGGG AAGAAAACAA CGGCGACTGG GCAGCTGCCT CCACTTCTGA      60

CAACTCCAAA GGGATATACT TGTAGAAGTG GCTCGCAGGC TGGGGCTCCG CAGAGAGAGA     120

CCAGAAGGTG CCAACCGCAG AGGGGTGCAG ATATCTCCCC CTATTCCCCA CCCCACCTCC     180

CTTGGGTTTT GTTCACCGTG CTGTCATCTG TTTTTCAGAC CTTTTTGGCA TCTAACATGG     240

TGAAGAAAGG AGTAAAGAAG AGAACAAAGT AACTCCTGGG GGAGCGAAGA GCGCTGGTGA     300

CCAACACCAC CAACGCCACC ACCAGCTCCT GCTGCTGCGG CCACCCACGT CCACCATTTA     360

CCGGGAGGCT CCAGAGGCGT AGGCAGCGGA TCCGAGAAAG GAGCGAGGGG AGTCAGCCGG     420

CTTTTCCGAG GAGTTATGGA TGTTGGTGCA TTCACTTCTG GCCAGATCCG CGCCCAGAGG     480

GAGCTAACCA GCAGCCACCA CCTCGAGCTC TCTCCTTGCC TTGCATCGGG TCTTACCCTT     540

CCAGTATGTT CCTTCTGATG AGACAATTTC CAGTGCCGAG AGTTTCAGTA CA ATG          595
                                                            Met

TGG AAA TGG ATA CTG ACA CAT TGT GCC TCA GCC TTT CCC CAC CTG CCC       643
Trp Lys Trp Ile Leu Thr His Cys Ala Ser Ala Phe Pro His Leu Pro

GGC TGC TGC TGC TGC TGC TTT TTG TTG CTG TTC TTG GTG TCT TCC GTC       691
Gly Cys Cys Cys Cys Cys Phe Leu Leu Leu Phe Leu Val Ser Ser Val

CCT GTC ACC TGC CAA GCC CTT GGT CAG GAC ATG GTG TCA CCA GAG GCC       739
Pro Val Thr Cys Gln Ala Leu Gly Gln Asp Met Val Ser Pro Glu Ala

ACC AAC TCT TCT TCC TCC TCC TTC TCC TCT CCT TCC AGC GCG GGA AGG       787
Thr Asn Ser Ser Ser Ser Ser Phe Ser Ser Pro Ser Ser Ala Gly Arg

CAT GTG CGG AGC TAC AAT CAC CTT CAA GGA GAT GTC CGC TGG AGA AAG       835
His Val Arg Ser Tyr Asn His Leu Gln Gly Asp Val Arg Trp Arg Lys

CTA TTC TCT TTC ACC AAG TAC TTT CTC AAG ATT GAG AAG AAC GGG AAG       883
Leu Phe Ser Phe Thr Lys Tyr Phe Leu Lys Ile Glu Lys Asn Gly Lys

GTC AGC GGG ACC AAG AAG GAG AAC TGC CCG TAC AGC ATC CTG GAG ATA       931
Val Ser Gly Thr Lys Lys Glu Asn Cys Pro Tyr Ser Ile Leu Glu Ile

ACA TCA GTA GAA ATC GGA GTT GTT GCC GTC AAA GCC ATT AAC AGC AAC       979
Thr Ser Val Glu Ile Gly Val Val Ala Val Lys Ala Ile Asn Ser Asn

TAT TAC TTA GCC ATG AAC AAG AAG GGG AAA CTC TAT GGC TCA AAA GAA      1027
Tyr Tyr Leu Ala Met Asn Lys Lys Gly Lys Leu Tyr Gly Ser Lys Glu

TTT AAC AAT GAC TGT AAG CTG AAG GAG AGG ATA GAG GAA AAT GGA TAC      1075
Phe Asn Asn Asp Cys Lys Leu Lys Glu Arg Ile Glu Glu Asn Gly Tyr
```

FIG.3A

```
AAT ACC TAT GCA TCA TTT AAC TGG CAG CAT AAT GGG AGG CAA ATG TAT      1123
Asn Thr Tyr Ala Ser Phe Asn Trp Gln His Asn Gly Arg Gln Met Tyr

GTG GCA TTG AAT GGA AAA GGA GCT CCA AGG AGA GGA CAG AAA ACA CGA      1171
Val Ala Leu Asn Gly Lys Gly Ala Pro Arg Arg Gly Gln Lys Thr Arg

AGG AAA AAC ACC TCT GCT CAC TTT CTT CCA ATG GTG GTA CAC TCA          1216
Arg Lys Asn Thr Ser Ala His Phe Leu Pro Met Val Val His Ser

TAGAGGAAGG CAACGTTTGT GGATGCAGTA AAACCAATGG CTCTTTTGCC AAGAATAGTG   1276

GATATTCTTC ATGAAGACAG TAGATTGAAA GGCAAAGACA CGTTGCAGAT GTCTGCTTGC   1336

TTAAAAGAAA GCCAGCCTTT GAAGGTTTTT GTATTCACTG CTGACATATG ATGTTCTTTT   1396

AATTAGTTCT GTGTCATGTC TTATAATCAA GATATAGGCA GATCGAATGG GATAGAAGTT   1456

ATTCCCAAGT GAAAAACATT GTGGCTGGGT TTTTTGTTGT TGTTGTCAAG TTTTTGTTTT   1516

TAAACCTCTG AGATAGAACT TAAAGGACAT AGAACAATCT GTTGAAAGAA CGATCTTCGG   1576

GAAAGTTATT TATGGAATAC GAACTCATAT CAAAGACTTC ATTGCTCATT CAAGCCTAAT   1636

GAATCAATGA ACAGTAATAC GTGCAAGCAT TTACTGGAAA GCACTTGGGT CATATCATAT   1696

GCACAACCAA AGGAGTTCTG GATGTGGTCT CATGGAATAA TTGAATAGAA TTTAAAAATA   1756

TAAACATGTT AGTGTGAAAC TGTTCTAACA ATACAAATAG TATGGTATGC TTGTGCATTC   1816

TGCCTTCATC CCTTTCTATT TCTTTCTAAG TTATTTATTT AATAGGATGT TAAATATCTT   1876

TTGGGGTTTT AAAGAGTATC TCAGCAGCTG TCTTCTGATT TATCTTTTCT TTTTATTCAG   1936

CACACCACAT GCATGTTCAC GACAAAGTGT TTTTAAAACT TGGCGAACAC TTCAAAAATA   1996

GGAGTTGGGA TTAGGGAAGC AGTATGAGTG CCCGTGTGCT ATCAGTTGAC TTAATTTGCA   2056

CTTCTGCAGT AATAACCATC AACAATAAAT ATGGCAATGC TGTGCCATGG CTTGAGTGAG   2116

AGATGTCTGC TATCATTTGA AAACATATAT TACTCTCGAG GCTTCCTGTC TCAAGAAATA   2176

GACCAGAAGG CCAAATTCTT CTCTTTCAAT ACATCAGTTT GCCTCCAAGA ATATACTAAA   2236

AAAAGGAAAA TTAATTGCTA AATACATTTA AATAGCCTAG CCTCATTATT TACTCATGAT   2296

TTCTTGCCAA ATGTCATGGC GGTAAAGAGG CTGTCCACAT CTCTAAAAAC CCTCTGTAAA   2356

TTCCACATAA TGCATCTTTC CCAAAGGAAC TATAAAGAAT TTGGTATGAA GCGCAACTCT   2416
```

FIG.3B

CCCAGGGGCT TAAACTGAGC AAATCAAATA TATACTGGTA TATGTGTAAC CATATACAAA 2476
AACCTGTTCT AGCTGTATGA TCTAGTCTTT ACAAAACCAA ATAAAACTTG TTTTCTGTAA 2536
ATTTAAAGAG CTTTACAAGG TTCCATAATG TAACCATATC AAAATTCATT TTGTTAGAGC 2596
ACGTATAGAA AAGAGTACAT AAGAGTTTAC CAATCATCAT CACATTGTAT TCCACTAAAT 2656
AAATACATAA GCCTTATTTG CAGTGTCTGT AGTGATTTTA AAAATGTAGA AAAATACTAT 2716
TTGTTCTAAA TACTTTTAAG CAATAACTAT AATAGTATAT TGATGCTGCA GTTTTATCTT 2776
CATATTTCTT GTTTTGAAAA AGCATTTTAT TGTTTGGACA CAGTATTTTG GTACAAAAAA 2836
AAAGACTCAC TAAATGTGTC TTACTAAAGT TTAACCTTTG GAAATGCTGG CGTTCTGTGA 2896
TTCTCCAACA AACTTATTTG TGTCAATACT TAACCAGCAC TTCCAGTTAA TCTGTTATTT 2956
TTAAAAATTG CTTTATTAAG AAATTTTTTG TATAATCCCA TAAAAGGTCA TATTTTTCCC 3016
ATTCTTCAAA AAAACTGTAT TTCAGAAGAA ACACATTTGA GGCACTGTCT TTTGGCTTAT 3076
AGTTTAAATT GCATTTCATC ATACTTTGCT TCCAACTTGC TTTTTGGCAA ATGAGATTAT 3136
AAAAATGTTT AATTTTTGTG GTTGGAATCT GGATGTTAAA ATTTAATTGG TAACTCAGTC 3196
TGTGAGCTAT AATGTAATGC ATTCCTATCC AAACTAGGTA TCTTTTTTTC CTTTATGTTG 3256
AAATAATAAT GGCACCTGAC ACATAGACAT AGACCACCCA CAACCTAAAT TAAATGTTTG 3316
GTAAGACAAA TACACATTGG ATGACCACAG TAACAGCAAA CAGGGCACAA ACTGGATTCT 3376
TATTTCACAT AGACATTTAG ATTACTAAAG AGGGCTATGT GTAAACAGTC ATCATTATAG 3436
TACTCAAGAC ACTAAAACAG CTTCTAGCCA AATATATTAA AGCTTGCAGA GGCCAAAAAT 3496
AGAAAACATC TCCCCTGTCT CTCCCACATT TCCCTCACAG AAAGACAAAA AACCTGCCTG 3556
GTGCAGTAGC TCACACCTGT AATCCCAGCA GTTTGGGAGA CTGTGGGAAG ATGGCTTGAG 3616
TCCAGGAGTT CTAGACAGGC CTGAGAAACC TAGTGAGACA TCCTTCTCTT AAACAAAACA 3676
AAACAAAACA AATGTAGCCA TGCGTGGTGG CATATACCTG TGGTCCCAAC TACTCAGGAG 3736
GCTGAAACGG AAGGATCTCT TGGGCCCCAG GAGTTTGAGG CTGCAGTGAG CTATAATCTT 3796
GCCATTGCAC TCCAGCCTGG GTGAAAAAGA GCCAGAAAGA AAGGAAAGAG AGAAAAGAGA 3856
AAAGAAAGAG AGAAAAGACA GAAAGACAGG AAGGAAGGAA GGAAGGAAGG AAGGAAGGAA 3916
GGAAGCAAGG AAAGAAGGAA GGAAGGAAAG AAGGGAGGGA AGGAAGGAGA GAGAAAGAAA 3976
GATTGTTTGG TAAGGAGTAA TGACATTCTC TTGCATTTAA AAGTGGCATA TTTGCTTGAA 4036

FIG.3C

```
ATGGAAATAG AATTCTGGTC CCTTTTGCAA CTACTGAAGA AAAAAAAAAG CAGTTTCAGC   4096
CCTGAATGTT GTAGATTTGA AAAAAAAAAA AAAAAAACTC GAGGGGGGGC CCGTACCCAA   4156
TTCGCCCTAT AGTGAGTCGT A                                             4177
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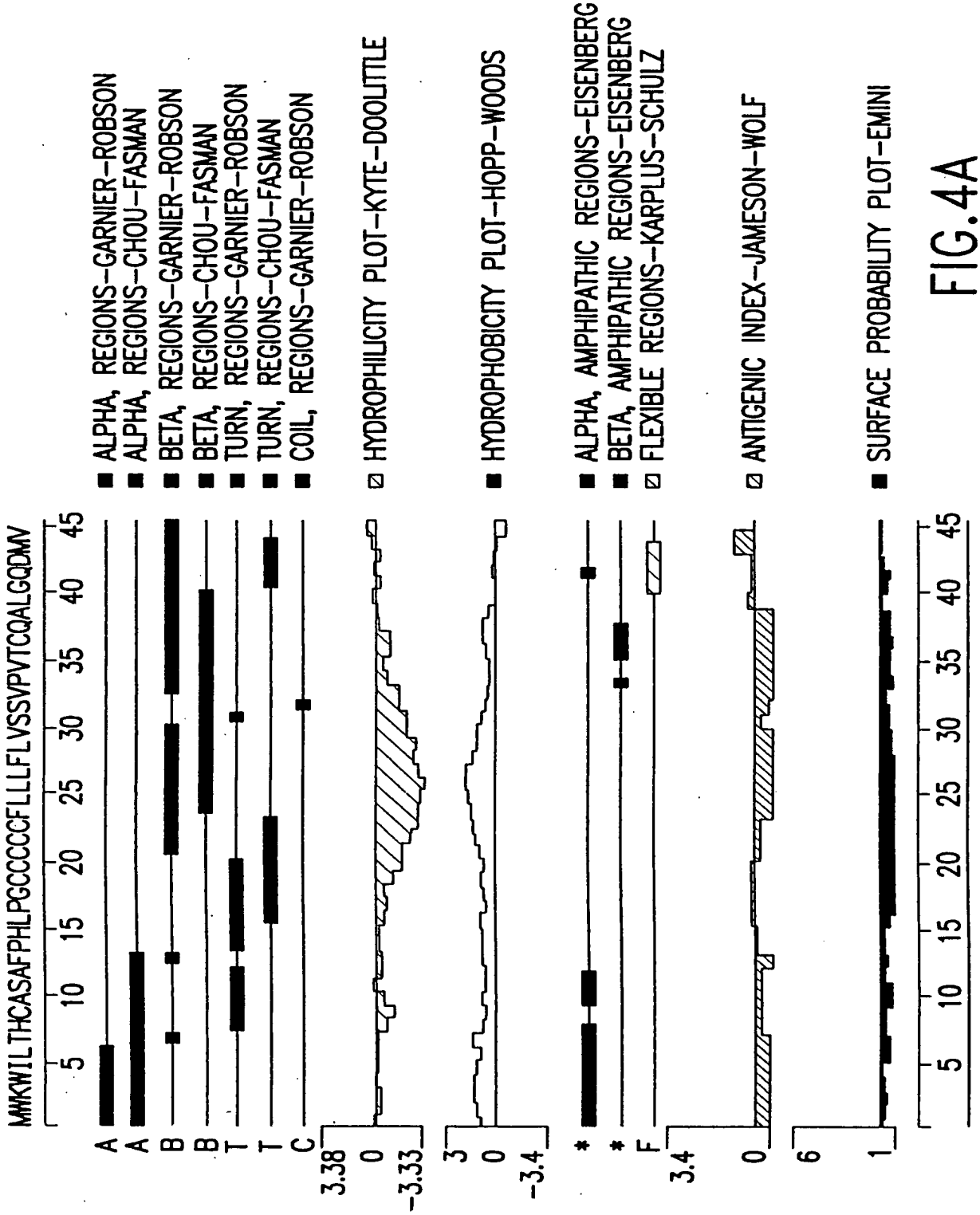
FIG.3D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A ALPHA, REGIONS-CHOU-FASMAN
B BETA, REGIONS-GARNIER-ROBSON
B BETA, REGIONS-CHOU-FASMAN
T TURN, REGIONS-GARNIER-ROBSON
T TURN, REGIONS-CHOU-FASMAN
C COIL, REGIONS-GARNIER-ROBSON
HYDROPHILICITY PLOT-KYTE-DOOLITTLE
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-3.33
HYDROPHOBICITY PLOT-HOPP-WOODS
3
0
-3.4
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* BETA, AMPHIPATHIC REGIONS-EISENBERG
F FLEXIBLE REGIONS-KARPLUS-SCHULZ
3.4
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SURFACE PROBABILITY PLOT-EMINI
1
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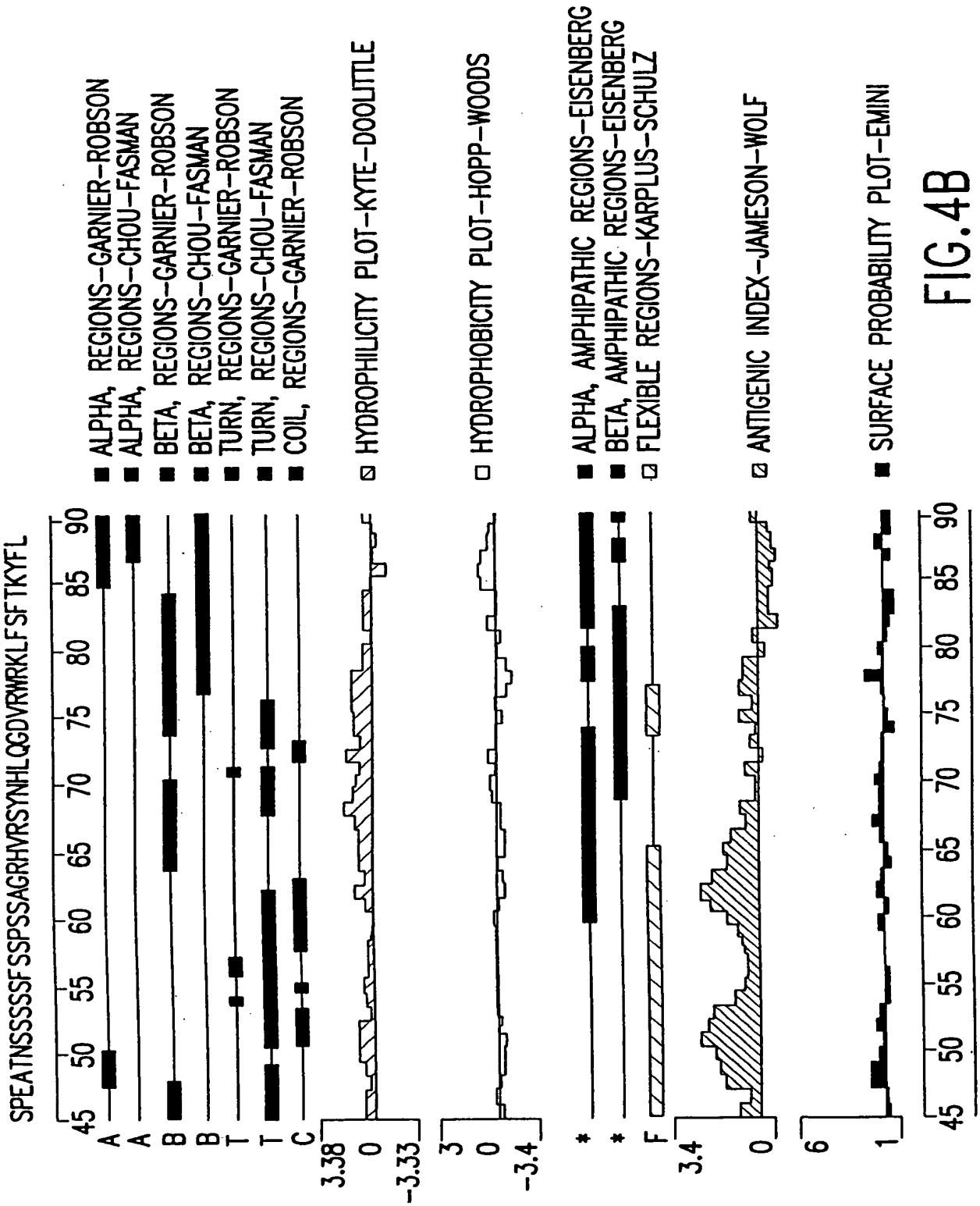
FIG.4A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B
B
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ALPHA, REGIONS-CHOU-FASMAN
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*
*
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BETA, AMPHIPATHIC REGIONS-EISENBERG
FLEXIBLE REGIONS-KARPLUS-SCHULZ
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6
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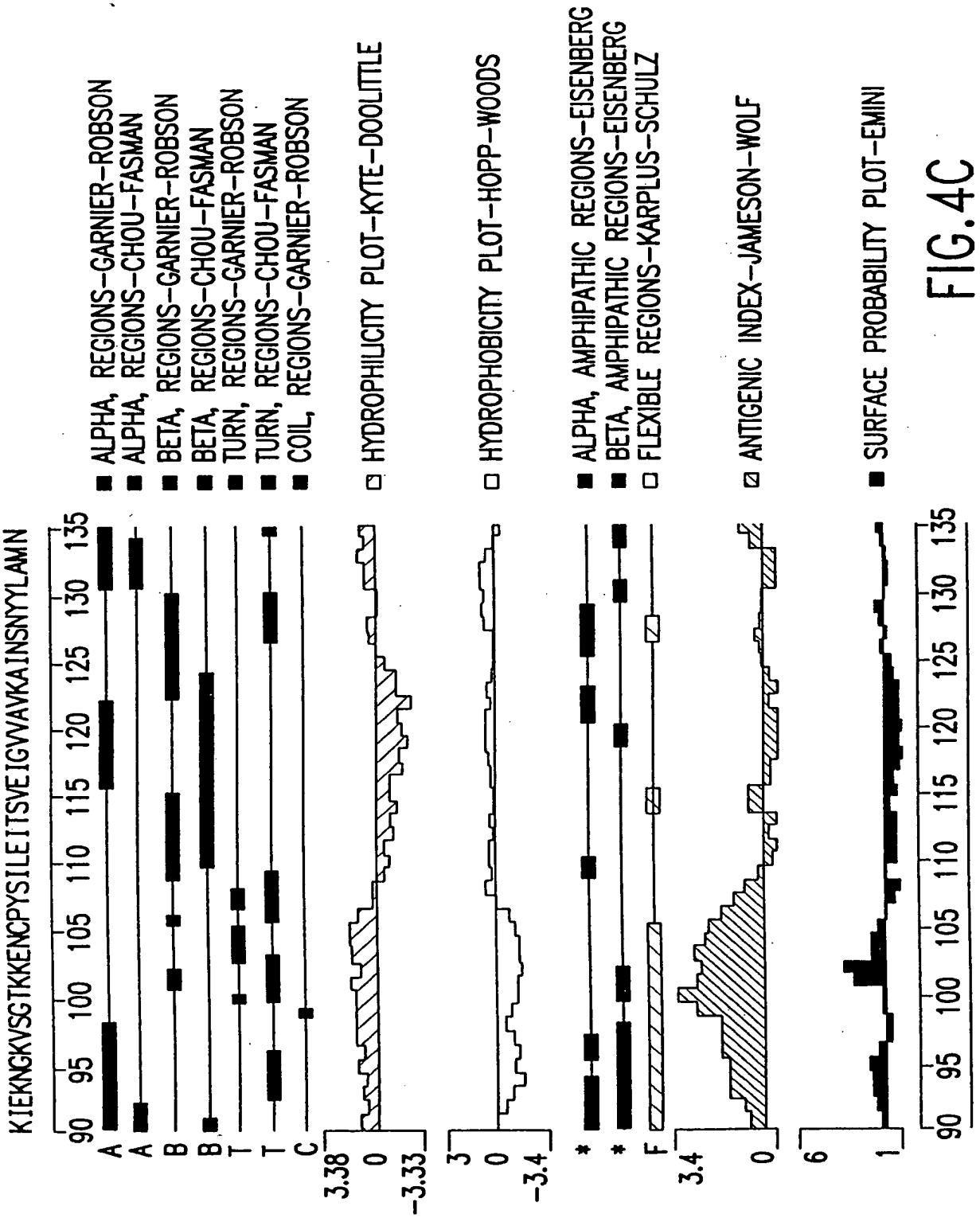
FIG.4B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C COIL, REGIONS-GARNIER-ROBSON
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-3.33
HYDROPHOBICITY PLOT-HOPP-WOODS
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ANTIGENIC INDEX-JAMESON-WOLF
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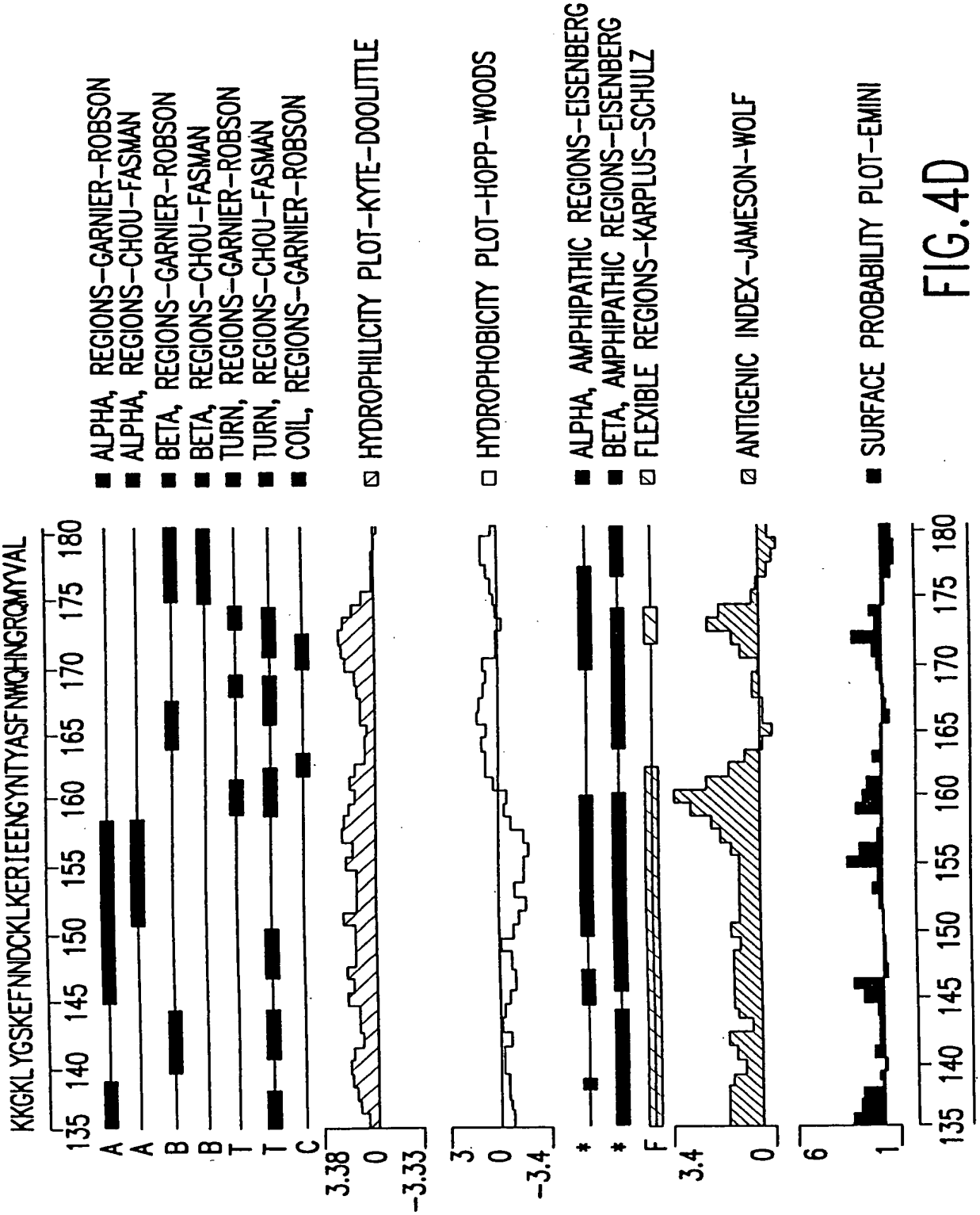
FIG.4C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A
B
B
T
T
C
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ALPHA, REGIONS-CHOU-FASMAN
BETA, REGIONS-GARNIER-ROBSON
BETA, REGIONS-CHOU-FASMAN
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TURN, REGIONS-CHOU-FASMAN
COIL, REGIONS-GARNIER-ROBSON
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3.38
0
-3.33
HYDROPHOBICITY PLOT-HOPP-WOODS
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BETA, AMPHIPATHIC REGIONS-EISENBERG
FLEXIBLE REGIONS-KARPLUS-SCHULZ
*
*
F
ANTIGENIC INDEX-JAMESON-WOLF
3.4
0
SURFACE PROBABILITY PLOT-EMINI
6
1
135 140 145 150 155 160 165 170 175 180

FIG.4D

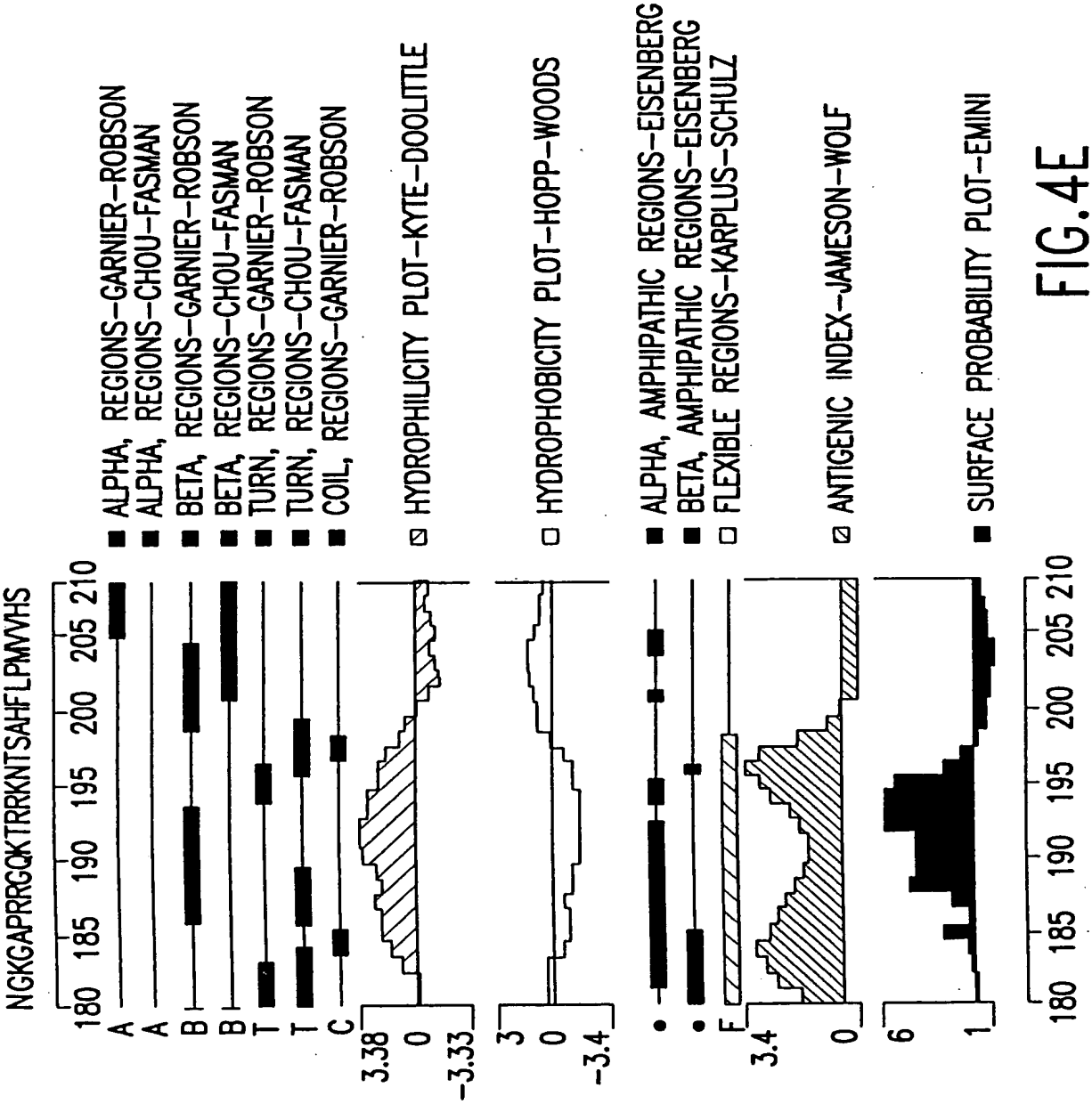

NGKGAPRRGQKTRRKNTSAHFLPMVVHS
180 185 190 195 200 205 210
A
A
B
B
T
T
C
ALPHA, REGIONS-GARNIER-ROBSON
ALPHA, REGIONS-CHOU-FASMAN
BETA, REGIONS-GARNIER-ROBSON
BETA, REGIONS-CHOU-FASMAN
TURN, REGIONS-GARNIER-ROBSON
TURN, REGIONS-CHOU-FASMAN
COIL, REGIONS-GARNIER-ROBSON
HYDROPHILICITY PLOT-KYTE-DOOLITTLE
3.38
0
-3.33
HYDROPHOBICITY PLOT-HOPP-WOODS
3
0
-3.4
ALPHA, AMPHIPATHIC REGIONS-EISENBERG
BETA, AMPHIPATHIC REGIONS-EISENBERG
FLEXIBLE REGIONS-KARPLUS-SCHULZ
F
ANTIGENIC INDEX-JAMESON-WOLF
3.4
0
SURFACE PROBABILITY PLOT-EMINI
6
1
180 185 190 195 200 205 210

FIG.4E

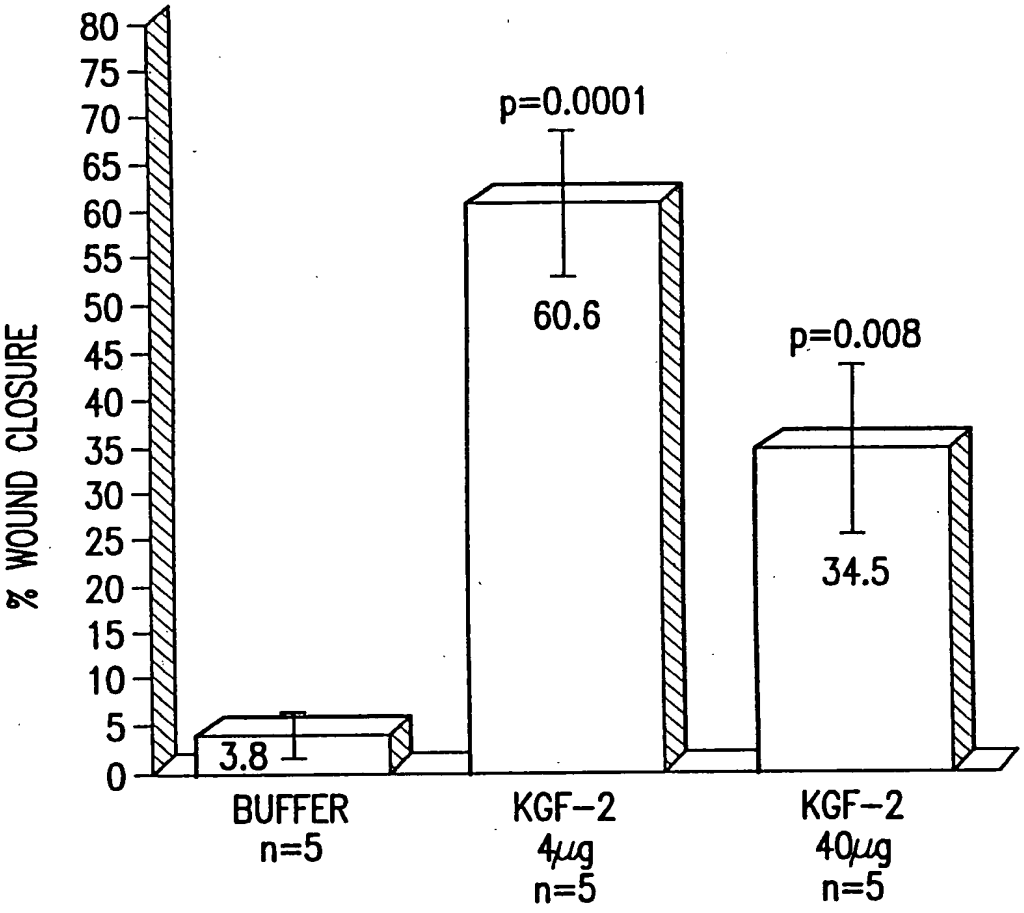

% WOUND CLOSURE
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
3.8
p=0.0001
60.6
p=0.008
34.5
BUFFER
n=5
KGF-2
4μg
n=5
KGF-2
40μg
n=5

FIG.5

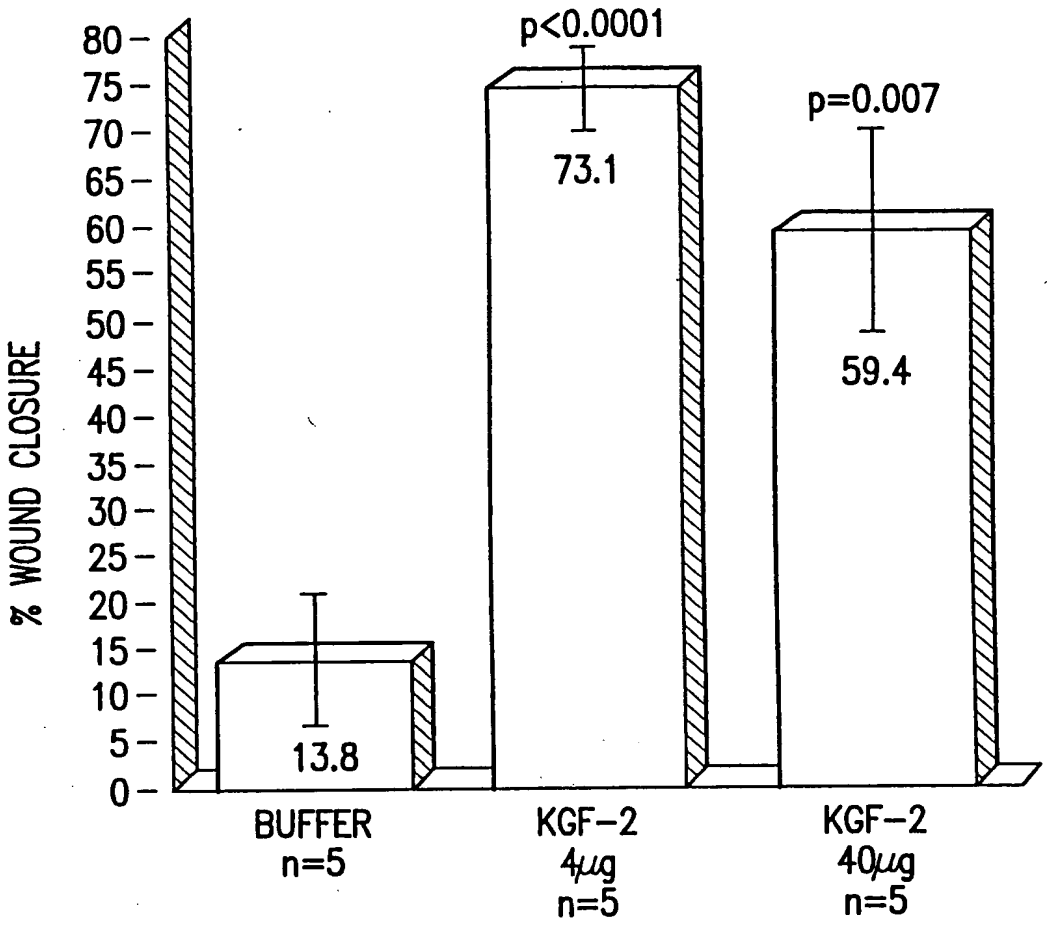

% WOUND CLOSURE
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
p<0.0001
73.1
p=0.007
59.4
13.8
BUFFER
n=5
KGF-2
4μg
n=5
KGF-2
40μg
n=5

FIG.6

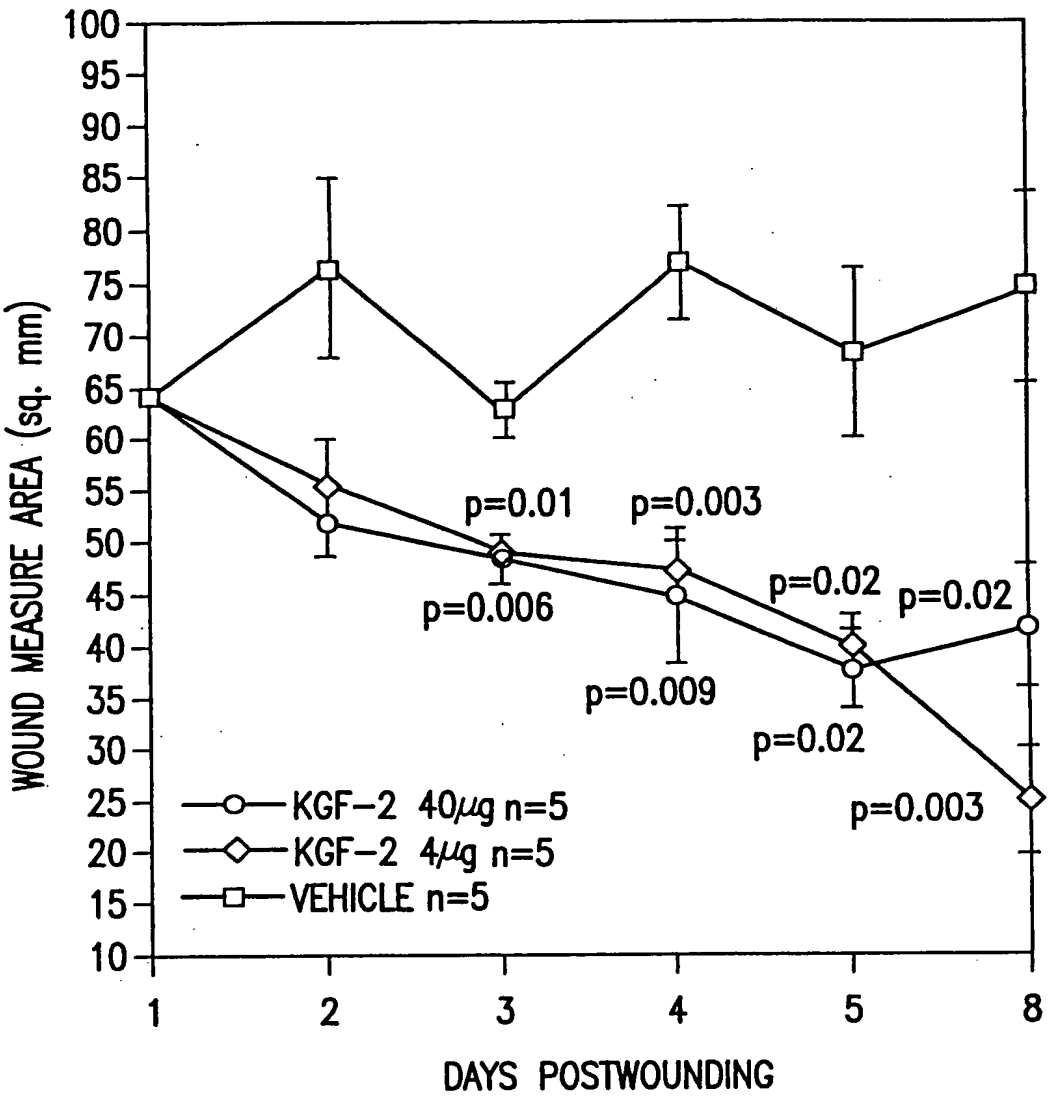

WOUND MEASURE AREA (sq. mm)
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
1
2
3
4
5
8
DAYS POSTWOUNDING
p=0.01
p=0.003
p=0.006
p=0.02
p=0.02
p=0.009
p=0.02
p=0.003
KGF-2 40μg n=5
KGF-2 4μg n=5
VEHICLE n=5

FIG.7

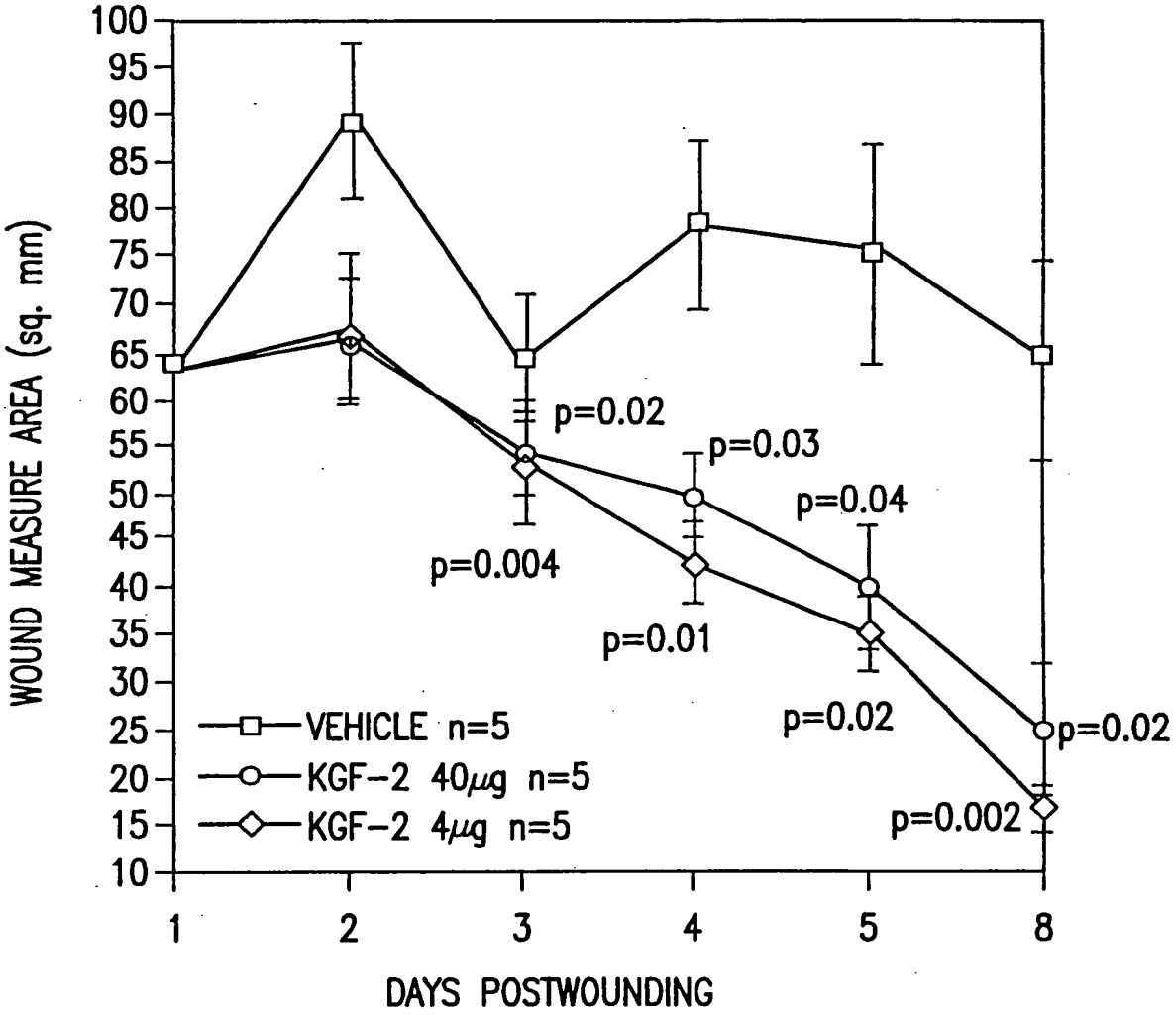
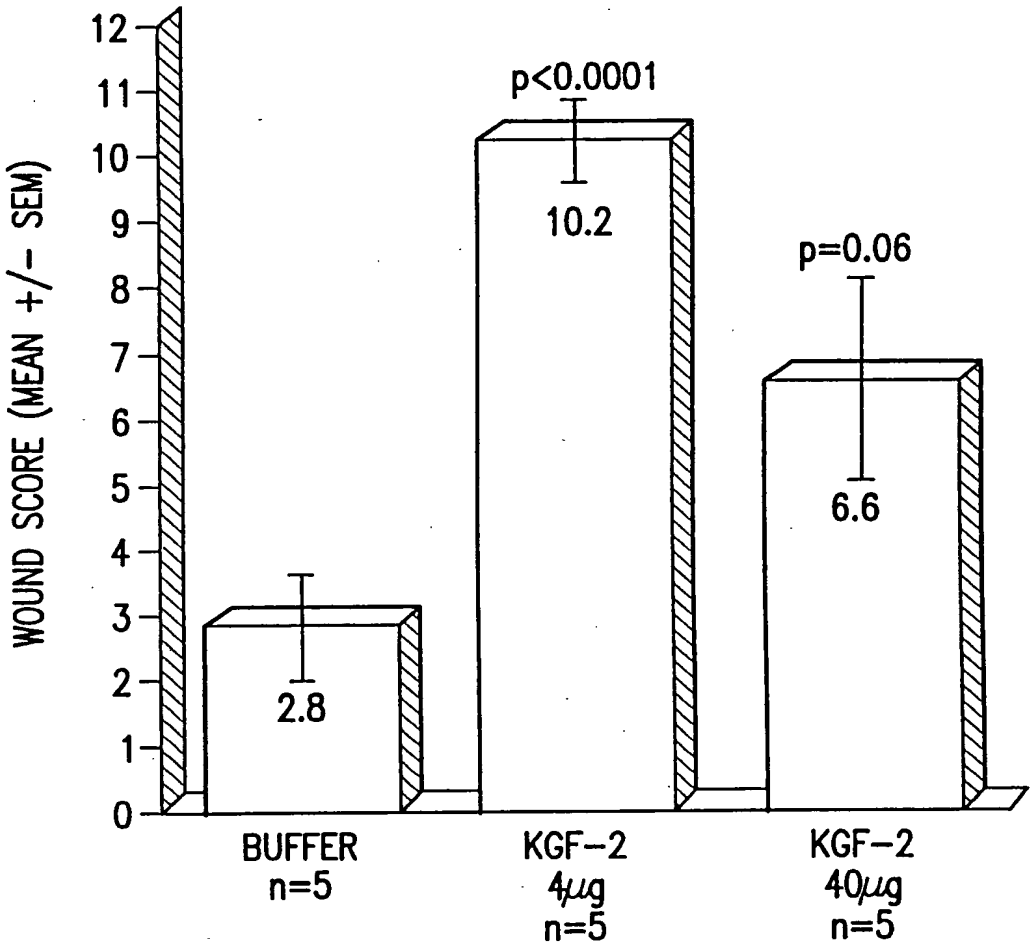
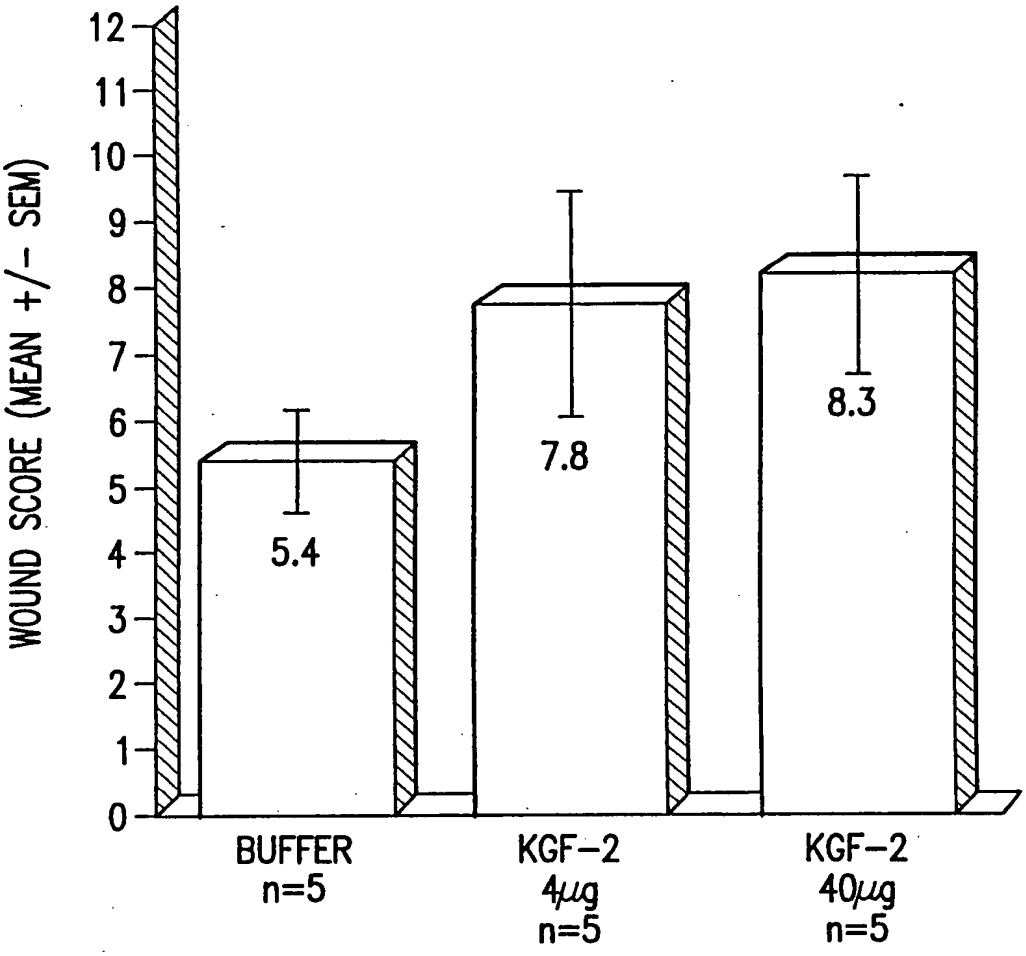

WOUND MEASURE AREA (sq. mm)
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
1
2
3
4
5
8
DAYS POSTWOUNDING
VEHICLE n=5
KGF-2 40μg n=5
KGF-2 4μg n=5
p=0.02
p=0.03
p=0.04
p=0.004
p=0.01
p=0.02
p=0.02
p=0.002

FIG.8



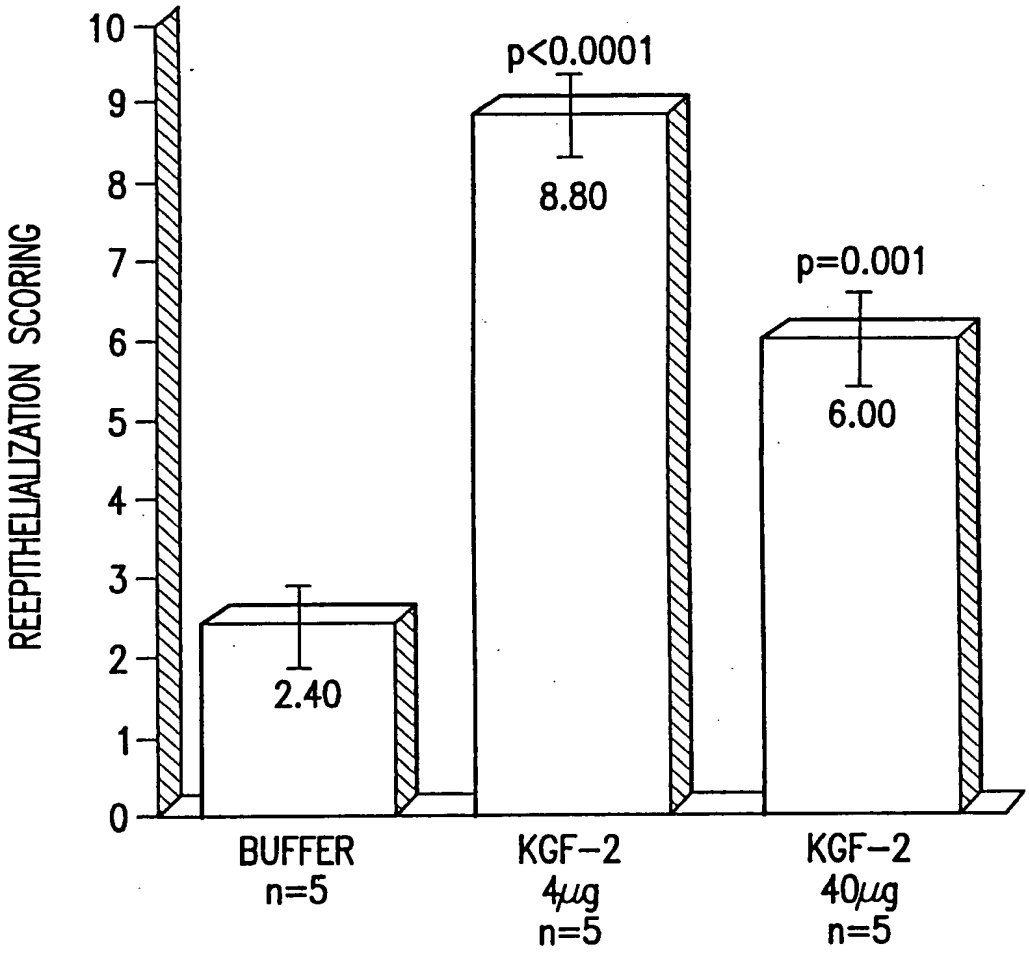
1-3 MINIMAL CELL ACCUMULATION, NO GRANULATION
4-6 IMMATURE GRANULATION, INFLAMMATORY CELLS, CAPILLARIES
10-12 FIBROBLASTS, COLLAGEN, EPITHELIUM

FIG.9



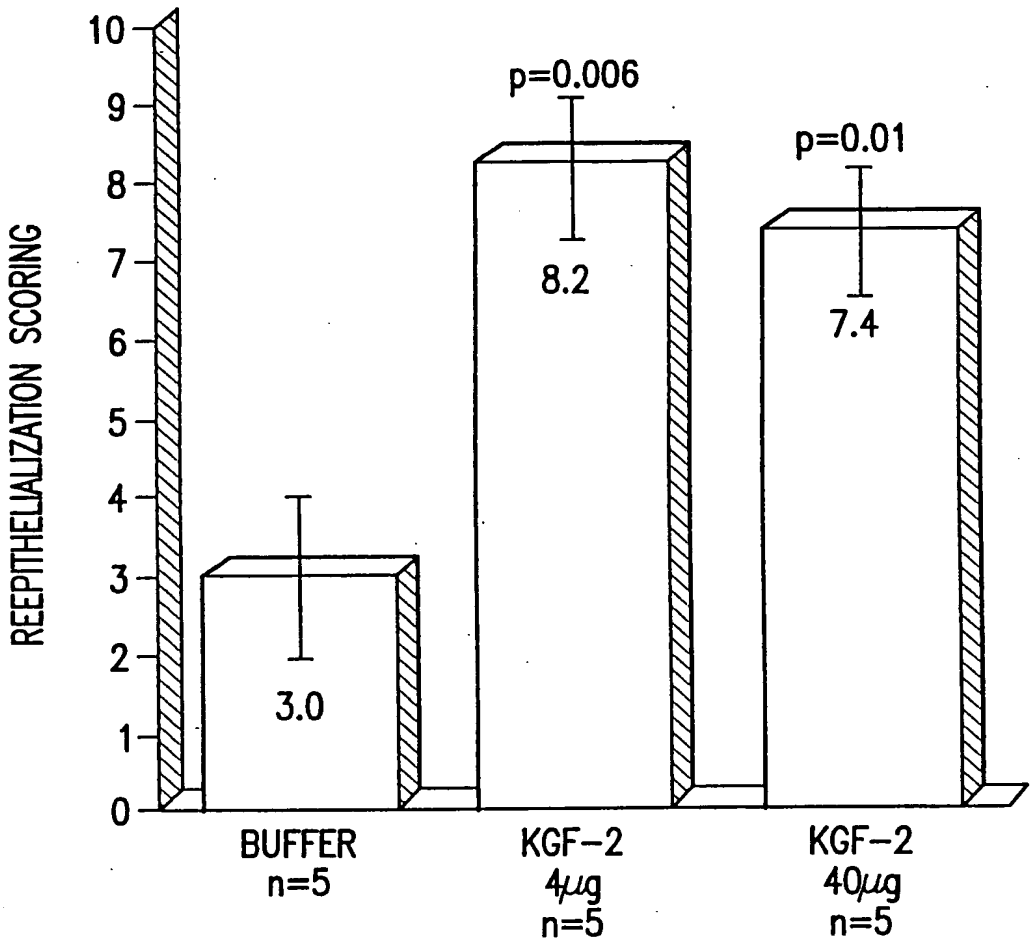
1-3 MINIMAL CELL ACCUMULATION, NO GRANULATION
4-6 IMMATURE GRANULATION, INFLAMMATORY CELLS, CAPILLARIES
7-9 GRANULATION TISSUE, CELLS, FIBROBLASTS, NEW EPITHELIUM
10-12 FIBROBLASTS, COLLAGEN, EPITHELIUM

FIG.10



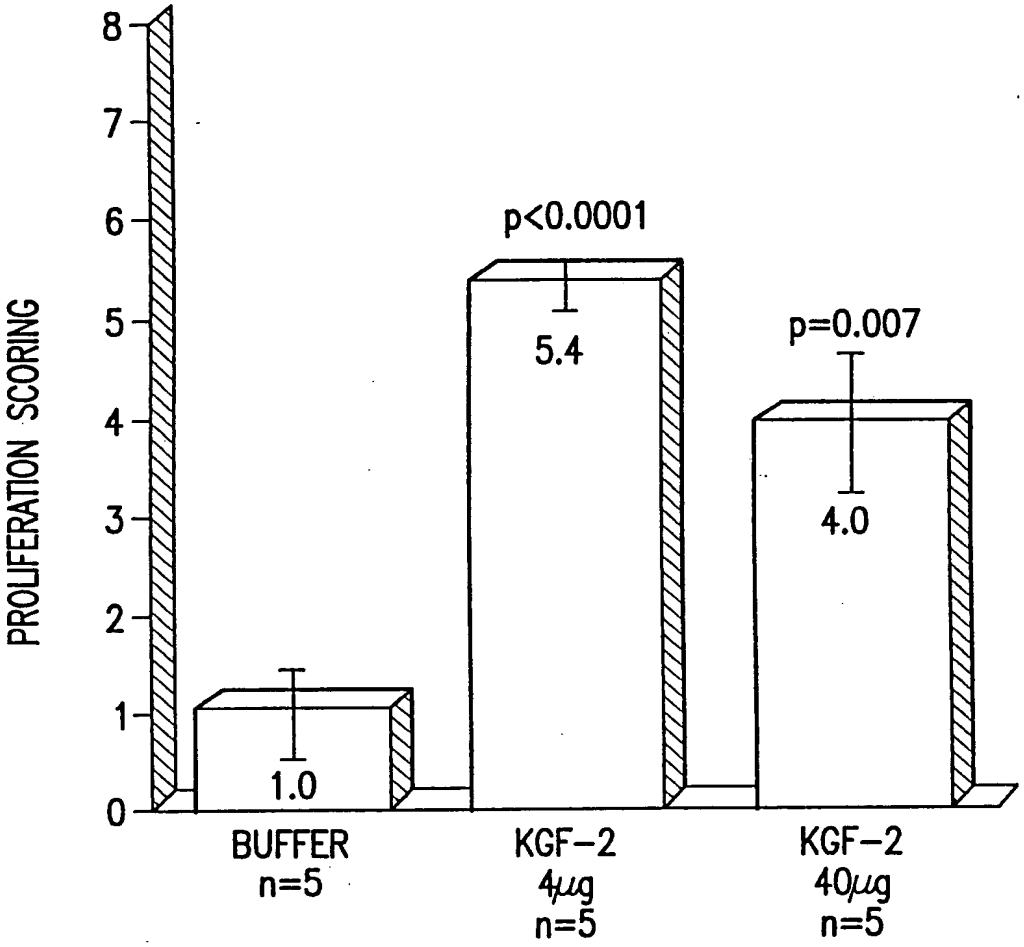
ANTI-CYTOKERATIN IMMUNOSTAINING
0-NO CLOSURE
5-SLIGHT TO MODERATE CLOSURE
10-COMPLETE CLOSURE

FIG.11



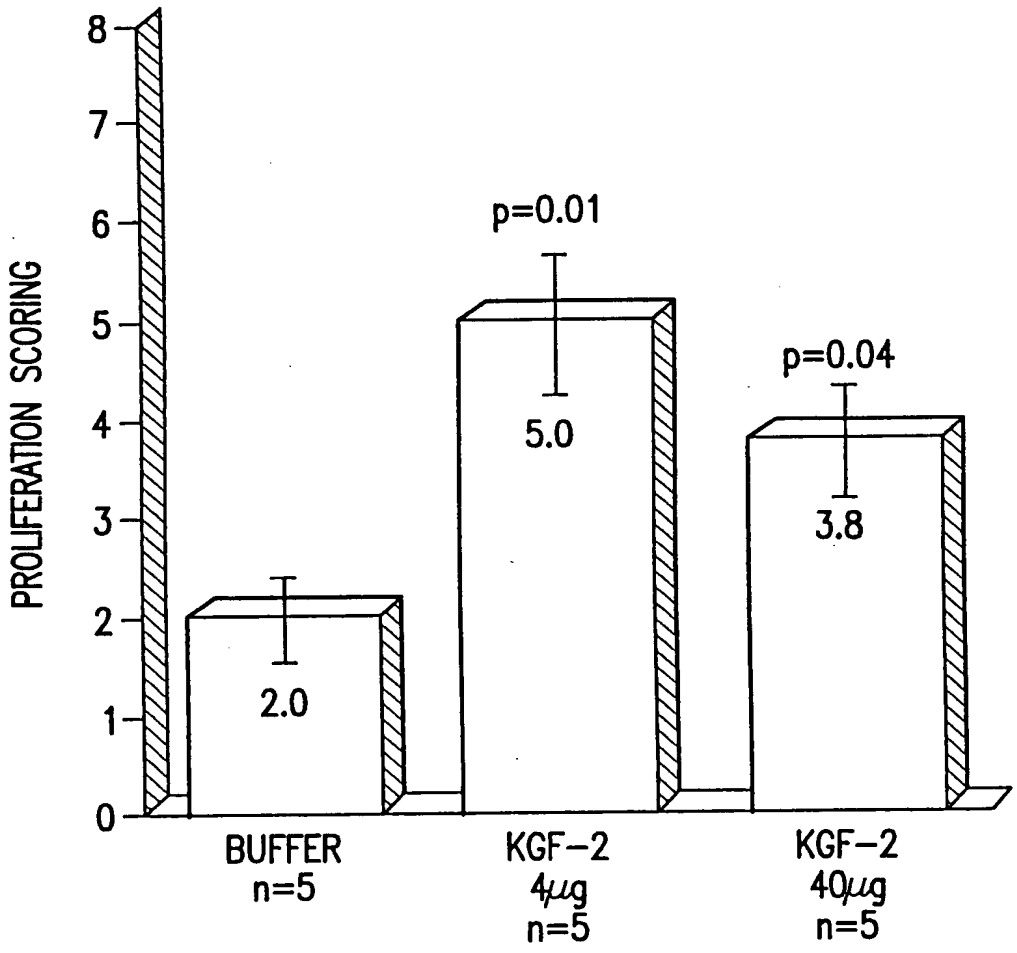
ANTI-CYTOKERATIN IMMUNOSTAINING
0-NO CLOSURE
5-SLIGHT TO MODERATE CLOSURE
10-COMPLETE CLOSURE

FIG.12



PCNA SCORING
0–2 SLIGHT PROLIFERATION
3–5 MODERATE PROLIFERATION
6–8 INTENSE PROLIFERATION

FIG.13



PCNA SCORING
0–2 SLIGHT PROLIFERATION
3–5 MODERATE PROLIFERATION
6–8 INTENSE PROLIFERATION

FIG.14

ATGAGAGGATCGCATCACCATCACCATCACGGATCCTGCCAGGCTCTGGGTC
AGGACATGGTTTCTCCGGAAGCTACCAACTCTTCCTCTTCCTCTTTCTCTTCCC
CGTCTTCCGCTGGTCGTCACGTTCGTTCTTACAACCACCTGCAGGGTGACGTTC
GTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAAATCGAAAAA
AACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCATCCTG
GAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAG
CAACTATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAG
AATTTAACAATGACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGAT
ACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGGCAAATGTAT
GTGGCATTGAaTGGAAAAGGAGCTCCAaGGAGAGGACAGAAAACACGAAG
GAAAAACACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCATAG

MRGSHHHHHHGSCQALGQDMVSPEATNSSSSSFSSPSSAGRHVRSYNHLQGD
VRWRKLFSFTKYFLKIEKNGKVSGTKKENCPYSILEITSVEIGVVAVKAINSN
YYLAMNKKGKLYGSKEFNNDCKLKERIEENGYNTYASFNWQHNGRQMYVA
LNGKGAPRRGQKTRRKNTSAHFLPMVVHS

kgf-2 synthetic cys37 Bam HI
AAAGGATCCTGCCAGGCTCTGGGTCAGGACATG

FIG.15

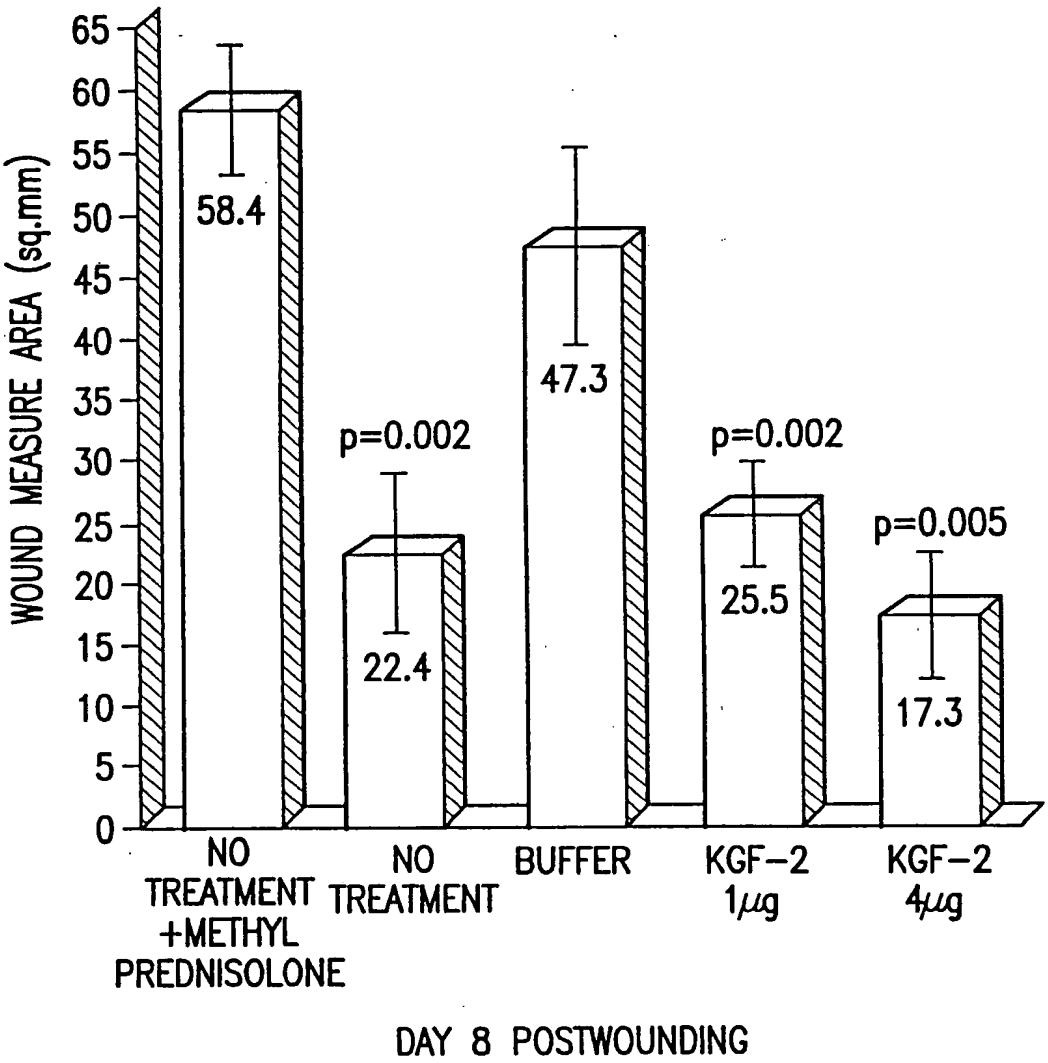

WOUND MEASURE AREA (sq.mm)
65
60
55
50
45
40
35
30
25
20
15
10
5
0
58.4
p=0.002
22.4
47.3
p=0.002
25.5
p=0.005
17.3
NO TREATMENT +METHYL PREDNISOLONE
NO TREATMENT
BUFFER
KGF-2 1μg
KGF-2 4μg
DAY 8 POSTWOUNDING

FIG.16

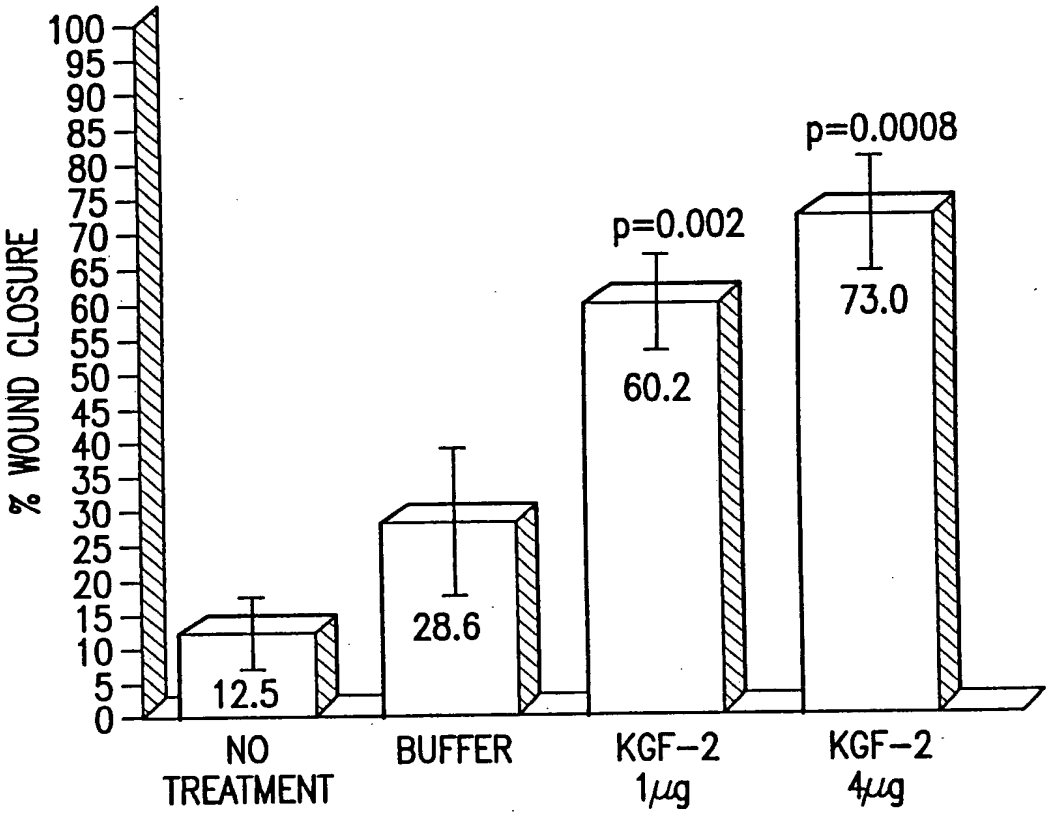

% WOUND CLOSURE
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
12.5
28.6
60.2
73.0
p=0.002
p=0.0008
NO TREATMENT
BUFFER
KGF-2 1μg
KGF-2 4μg
GLUCOCORTICOID TREATED ANIMALS

FIG.17

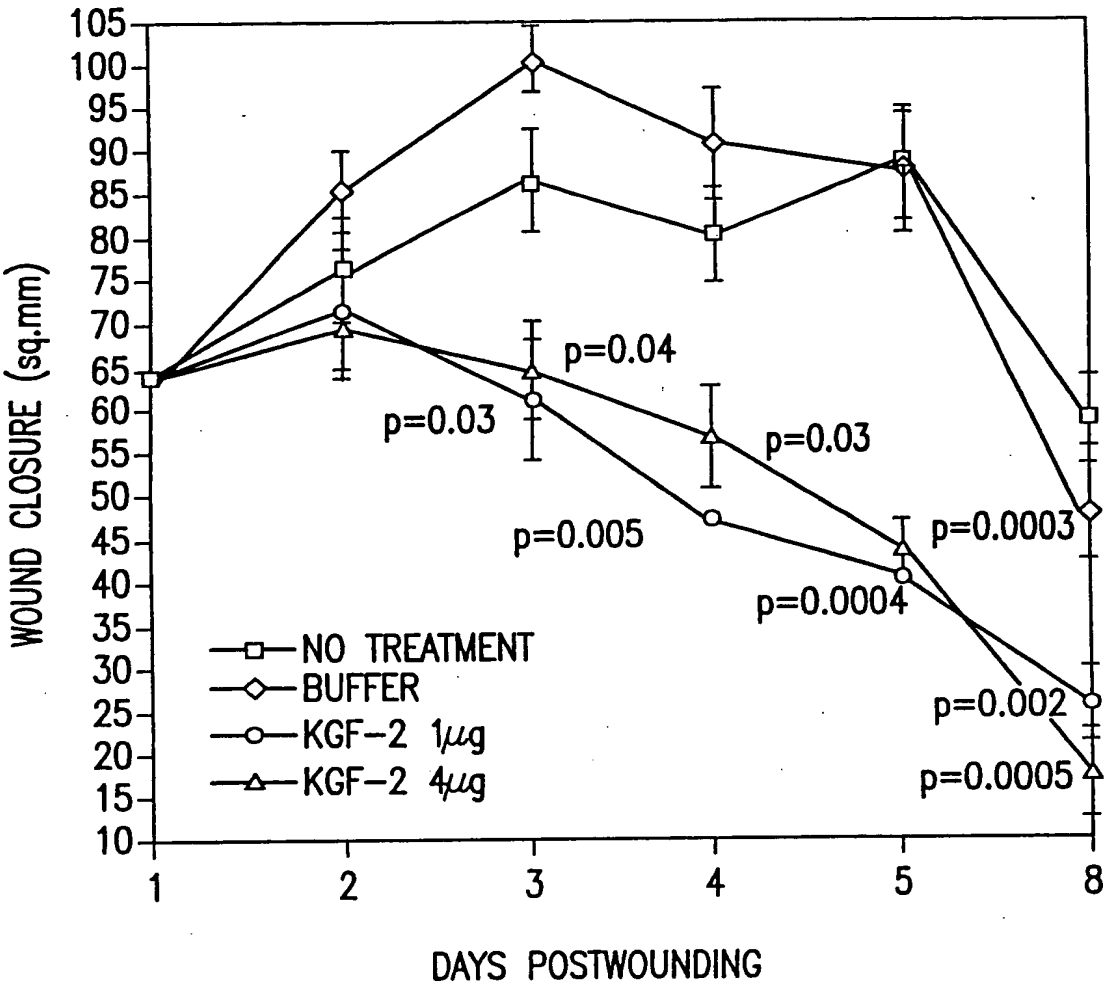

WOUND CLOSURE (sq.mm)
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
1
2
3
4
5
8
DAYS POSTWOUNDING
NO TREATMENT
BUFFER
KGF-2 1μg
KGF-2 4μg
p=0.04
p=0.03
p=0.03
p=0.005
p=0.0003
p=0.0004
p=0.002
p=0.0005

FIG.18

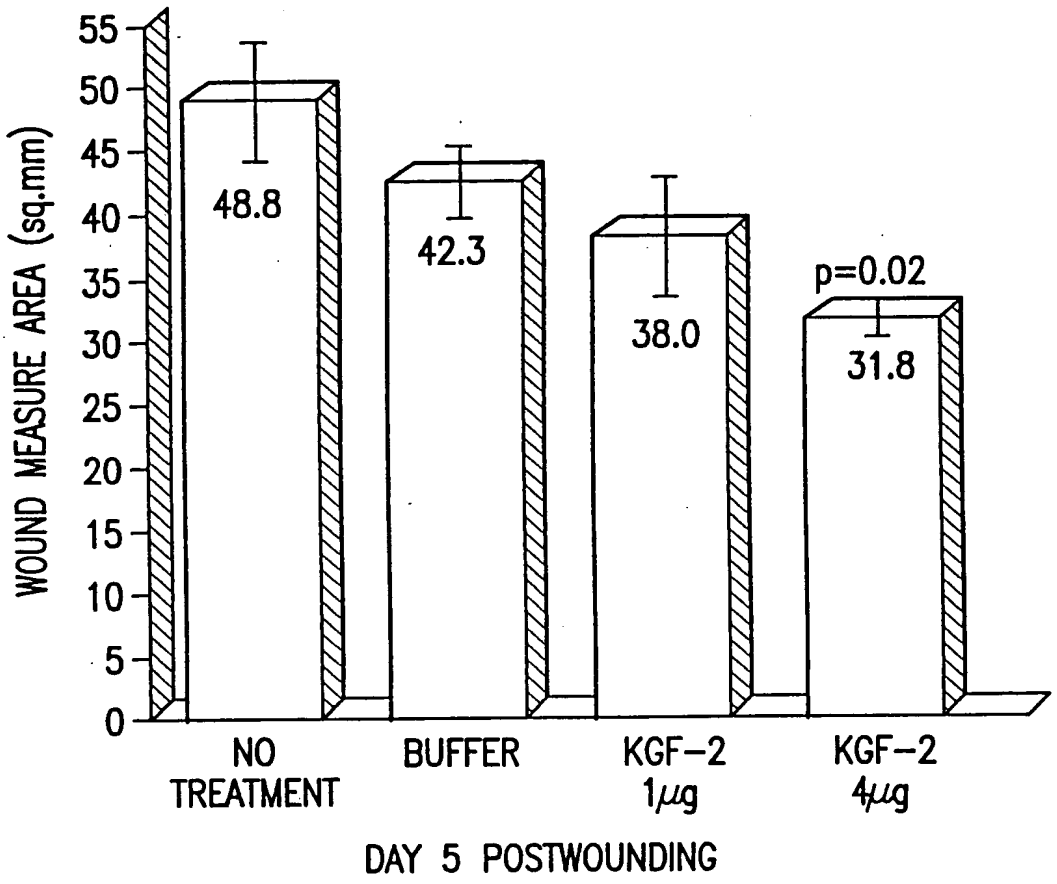

WOUND MEASURE AREA (sq.mm)
55
50
45
40
35
30
25
20
15
10
5
0
48.8
42.3
38.0
p=0.02
31.8
NO TREATMENT
BUFFER
KGF-2 1μg
KGF-2 4μg
DAY 5 POSTWOUNDING

FIG.19A

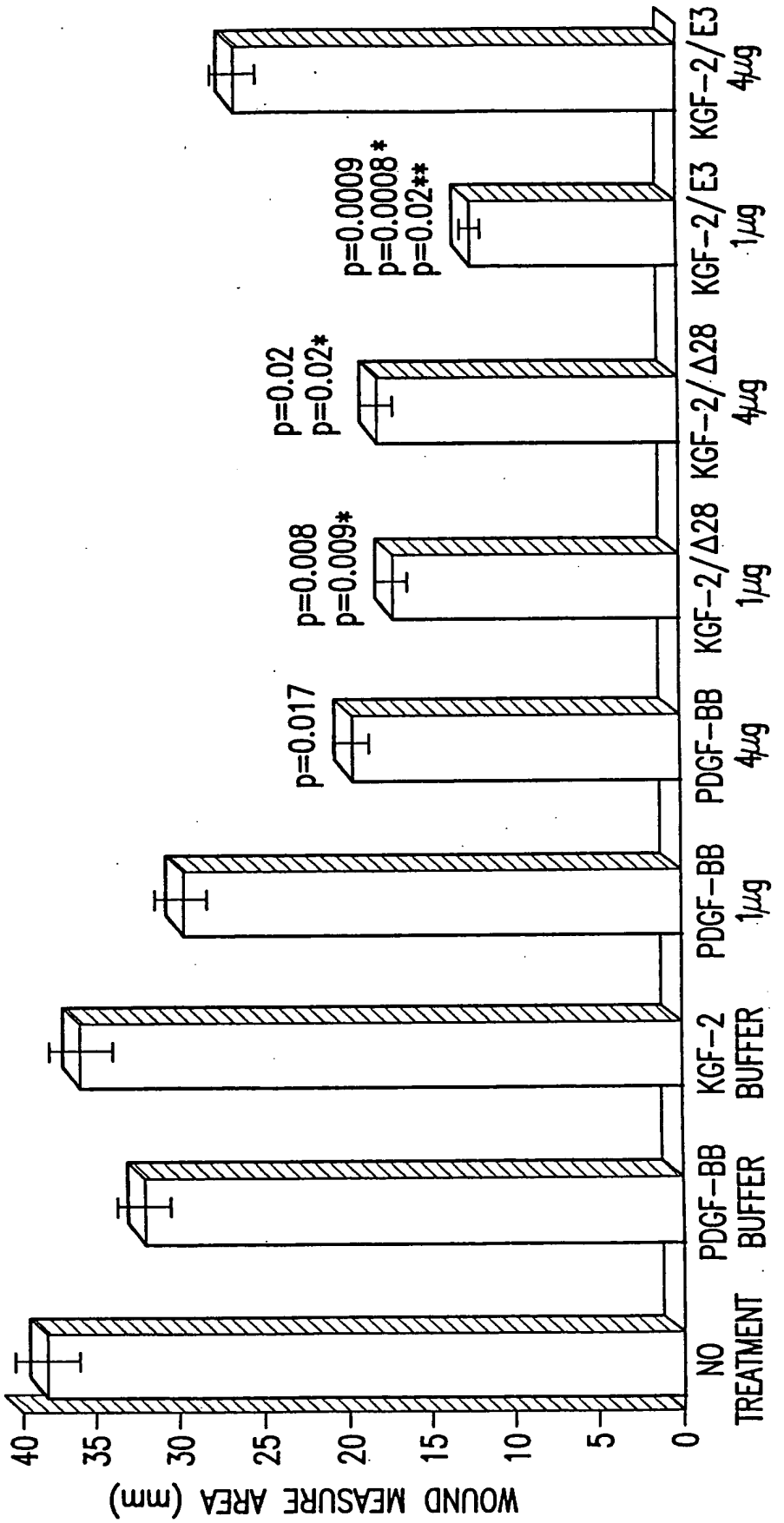

WOUND MEASURE AREA (mm)
40
35
30
25
20
15
10
5
0
NO TREATMENT
PDGF-BB BUFFER
KGF-2 BUFFER
PDGF-BB 1μg
PDGF-BB 4μg
KGF-2/Δ28 1μg
KGF-2/Δ28 4μg
KGF-2/E3 1μg
KGF-2/E3 4μg
p=0.017
p=0.008
p=0.009*
p=0.02
p=0.02*
p=0.0009
p=0.0008*
p=0.02**
DAY 10 POSTWOUNDING

FIG.19B

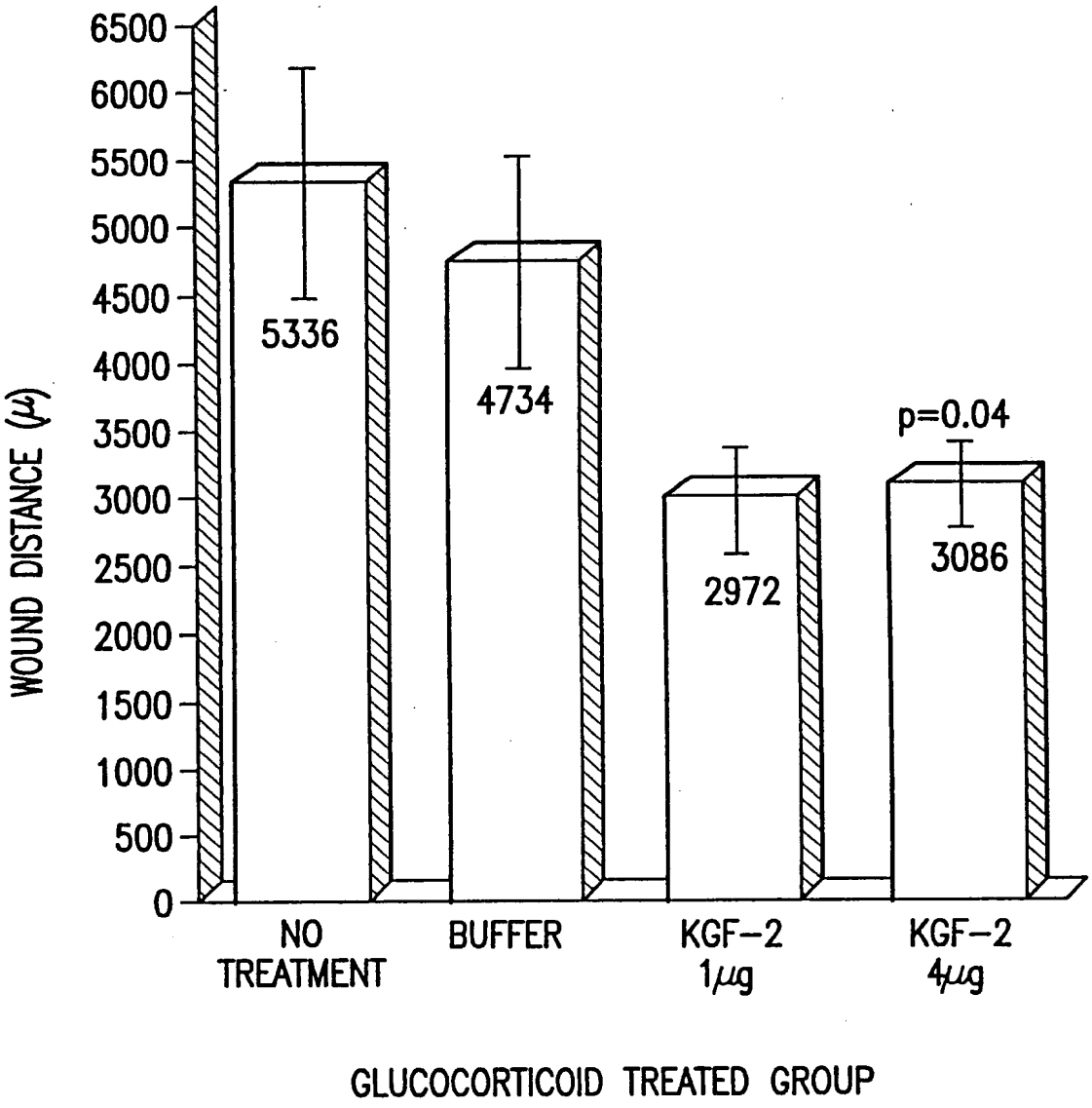

WOUND DISTANCE (μ)
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
5336
4734
2972
3086
p=0.04
NO TREATMENT
BUFFER
KGF-2 1μg
KGF-2 4μg
GLUCOCORTICOID TREATED GROUP

FIG.20

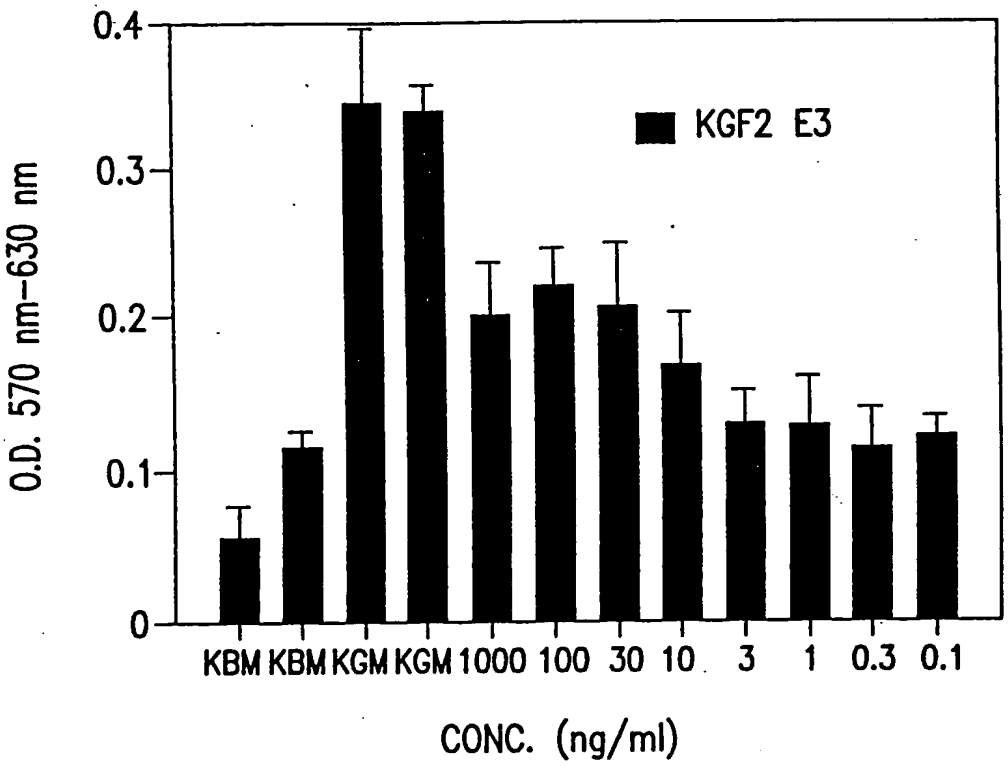


FIG.21A

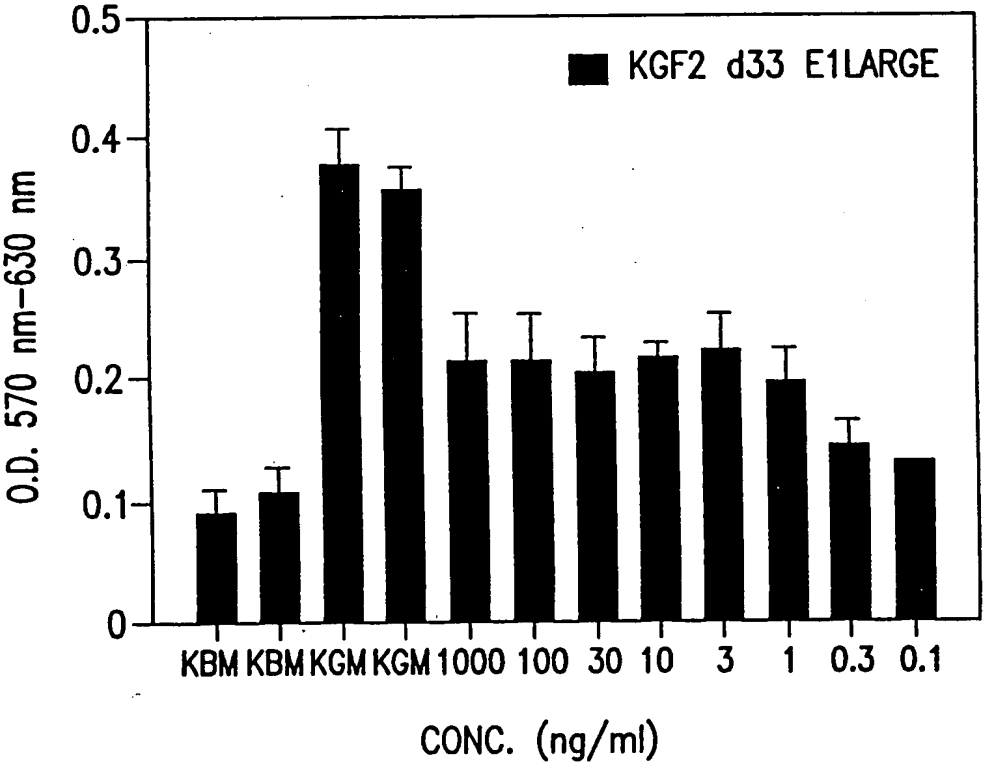
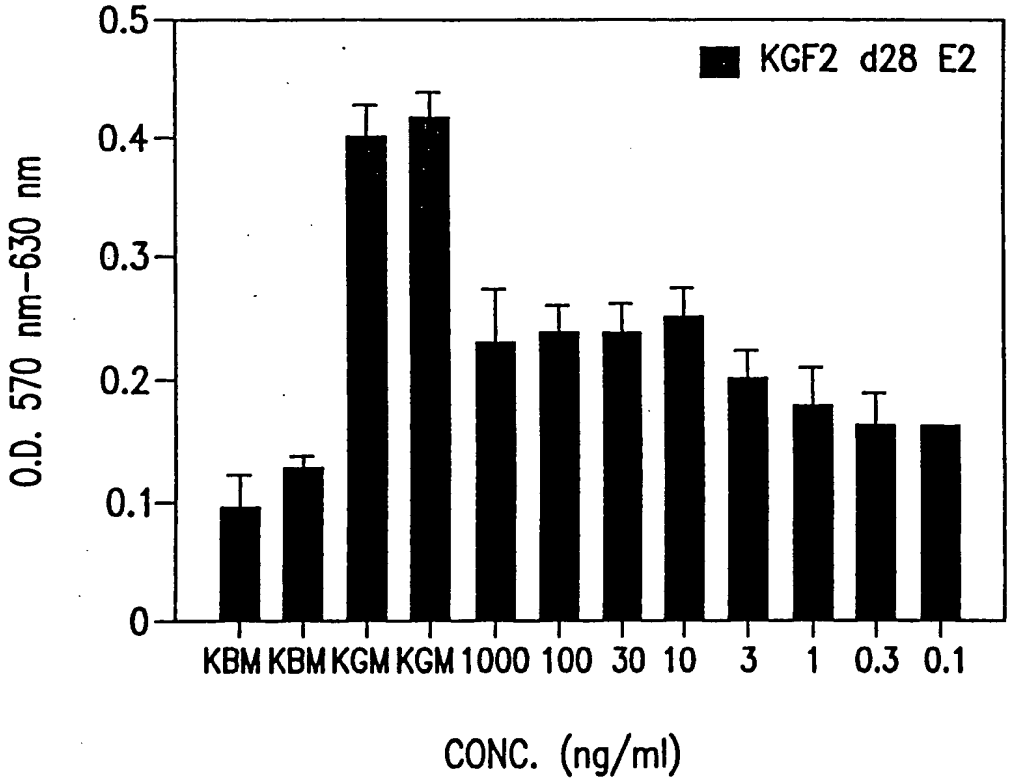


FIG.21B

BEST AVAILABLE COPY



BEST AVAILABLE COPY

FIG.21C

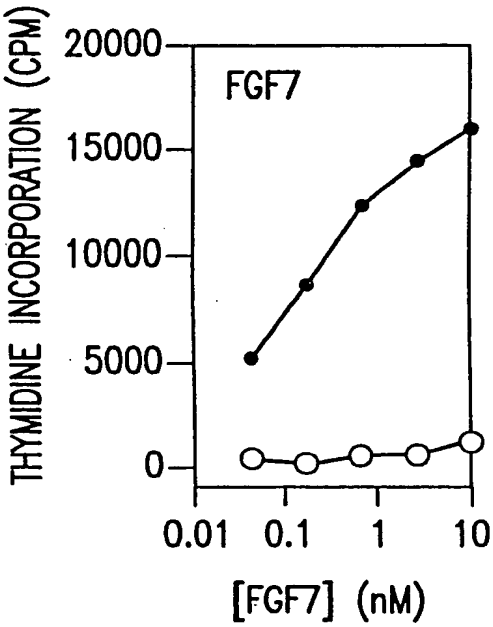


FIG.22A

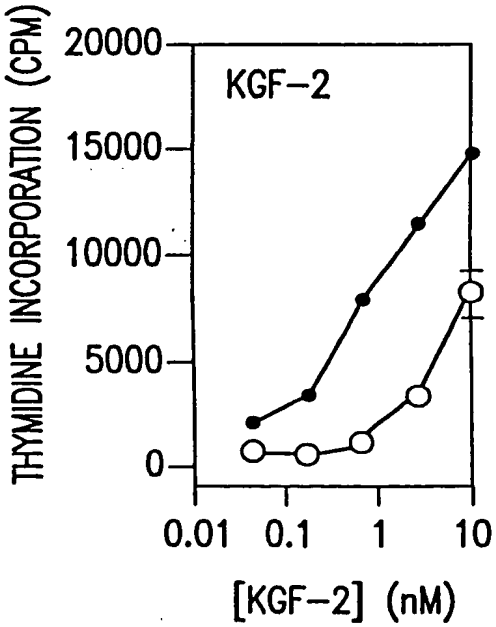


FIG.22A-1

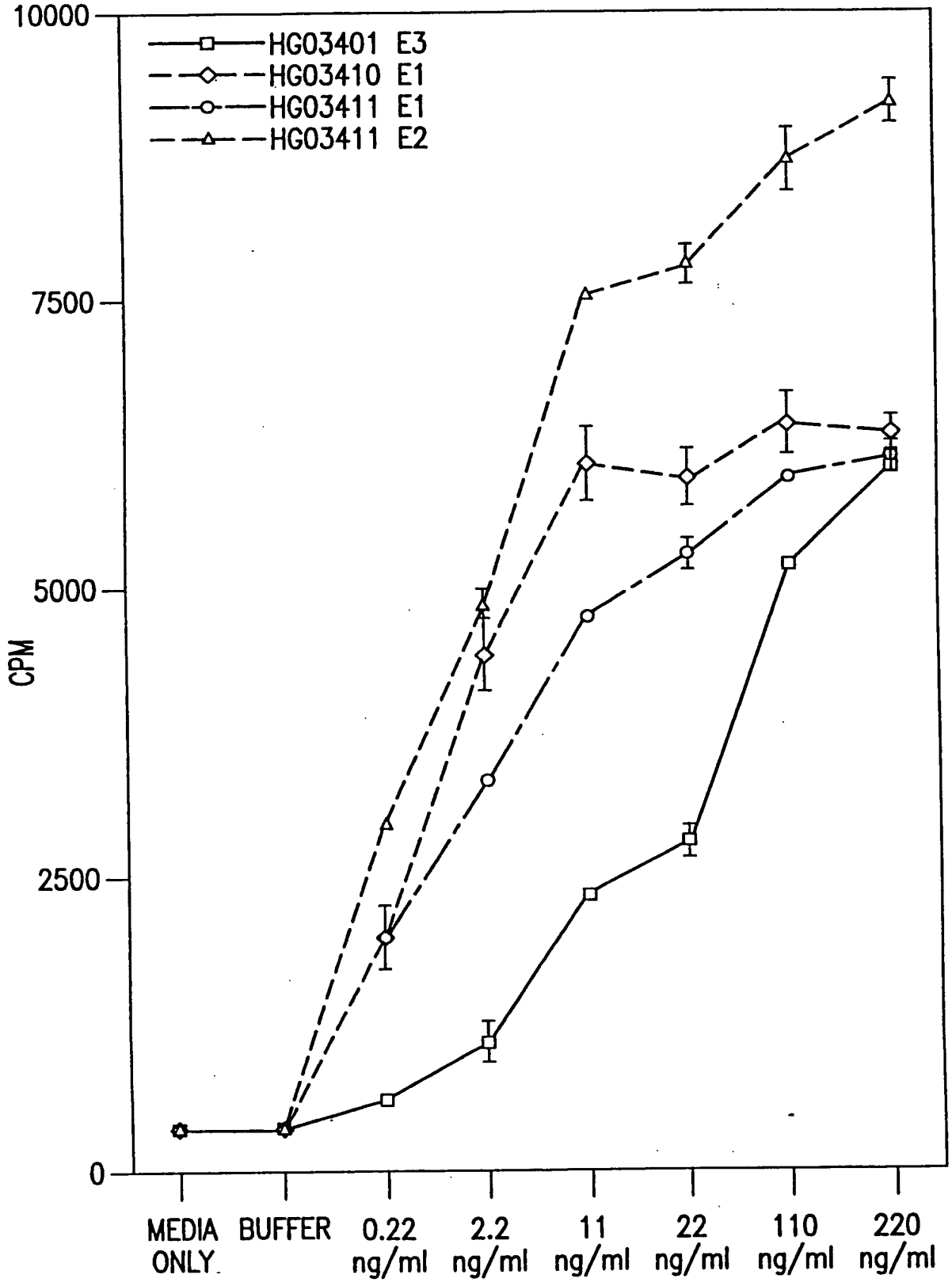

10000
7500
5000
2500
0
CPM
HG03401 E3
HG03410 E1
HG03411 E1
HG03411 E2
MEDIA ONLY
BUFFER
0.22 ng/ml
2.2 ng/ml
11 ng/ml
22 ng/ml
110 ng/ml
220 ng/ml

FIG.22B

BEST AVAILABLE COPY

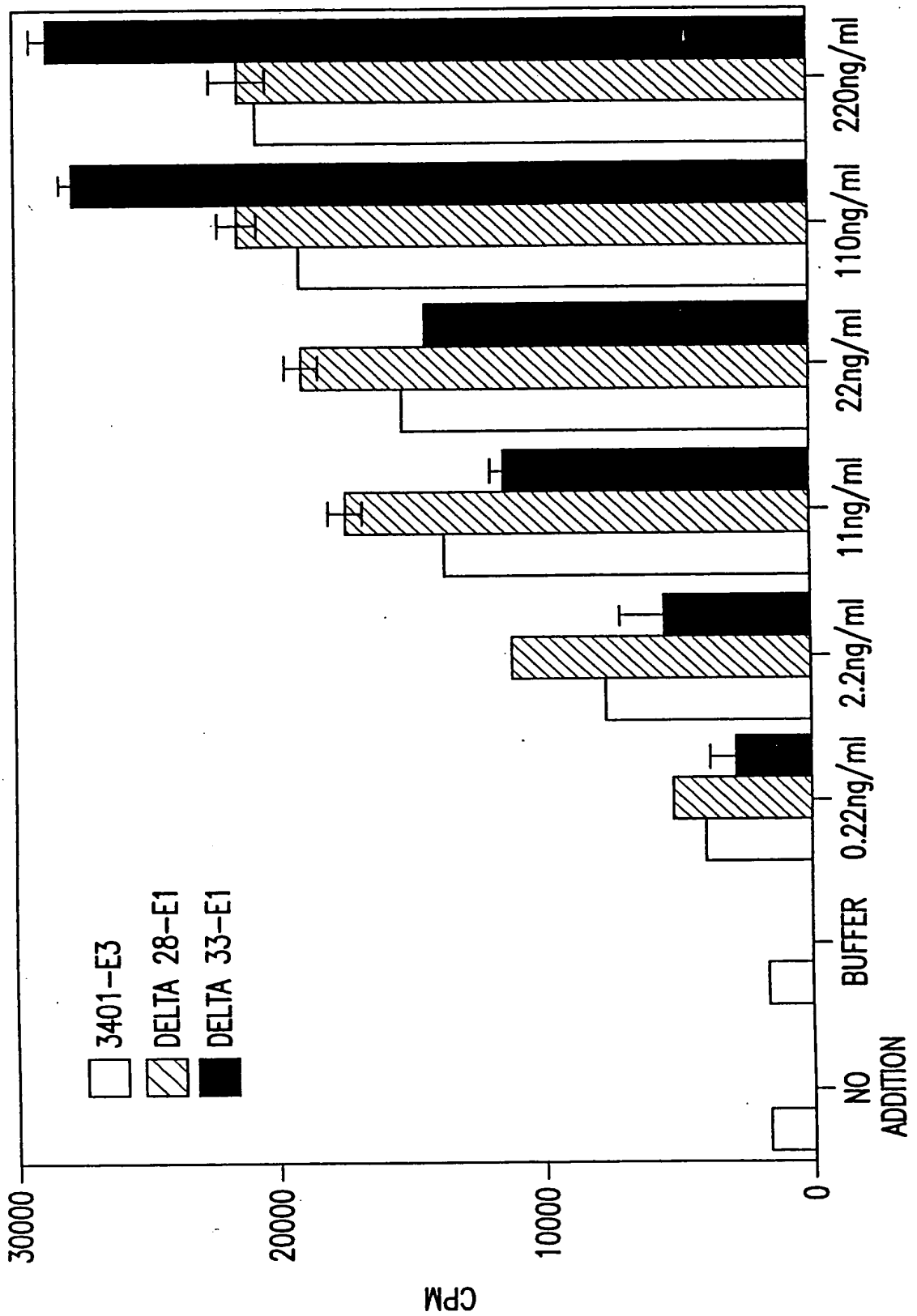


FIG.22C

ATGTGGAAATGGATACTGACCCACTGCGCTTCTGCTTTCCCGCACCTGCCGGGTTGCTGC 60
Met Trp Lys Trp Ile Leu Thr His Cys Ala Ser Ala Phe Pro His Leu Pro Gly Cys Cys
TGCTGCTGCTTCCTGCTGCTGTTCCTGGTTTCTTCTGTTCCGGTTACCTGCCAGGCTCTG 120
Cys Cys Cys Phe Leu Leu Leu Phe Leu Val Ser Ser Val Pro Val Thr Cys Gln Ala Leu
GGTCAGGACATGGTTTCTCCGGAAGCTACCAACTCTTCCTCTTCCTCTTTCTCTTCCCCG 180
Gly Gln Asp Met Val Ser Pro Glu Ala Thr Asn Ser Ser Ser Ser Ser Phe Ser Ser Pro
ACTTCCGCTGGTCGTCACGTTCGTTCTTACAACCACCTGCAGGGTGACGTTCGTTGGCGT 240
Thr Ser Ala Gly Arg His Val Arg Ser Tyr Asn His Leu Gln Gly Asp Val Arg Trp Arg
AAACTGTTCTCTTTCACCAAATACTTCCTGAAAATCGAAAAAAACGGTAAAGTTTCTGGG 300
Lys Leu Phe Ser Phe Thr Lys Tyr Phe Leu Lys Ile Glu Lys Asn Gly Lys Val Ser Gly
ACCAAGAAGGAGAACTGCCCGTACAGCATCCTGGAGATAACATCAGTAGAAATCGGAGTT 360
Thr Lys Lys Glu Asn Cys Pro Tyr Ser Ile Leu Glu Ile Thr Ser Val Glu Ile Gly Val
GTTGCCGTCAAAGCCATTAACAGCAACTATTACTTAGCCATGAACAAGAAGGGGAAACTC 420
Val Ala Val Lys Ala Ile Asn Ser Asn Tyr Tyr Leu Ala Met Asn Lys Lys Gly Lys Leu
TATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGA 480
Tyr Gly Ser Lys Glu Phe Asn Asn Asp Cys Lys Leu Lys Glu Arg Ile Glu Glu Asn Gly
TACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGGCAAATGTATGTGGCATTG 540
Tyr Asn Thr Tyr Ala Ser Phe Asn Trp Gln His Asn Gly Arg Gln Met Tyr Val Ala Leu
AATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGGAAAAACACCTCTGCTCAC 600
Asn Gly Lys Gly Ala Pro Arg Arg Gly Gln Lys Thr Arg Arg Lys Asn Thr Ser Ala His
TTTCTTCCAATGGTGGTACACTCATAG 627
Phe Leu Pro Met Val Val His Ser *

FIG.23

```
ATGACCTGCCAGGCTCTGGGTCAGGACATGGTTTCTCCGGAAGCTACCAACTCTTCCTCT   60
MetThrCysGlnAlaLeuGlyGlnAspMetValSerProGluAlaThrAsnSerSerSer

TCCTCTTTCTCTTCCCCGTCTTCCGCTGGTCGTCACGTTCGTTCTTACAACCACCTGCAG  120
SerSerPheSerSerProSerSerAlaGlyArgHisValArgSerTyrAsnHisLeuGln

GGTGACGTTCGTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAAATCGAAAAA  180
GlyAspValArgTrpArgLysLeuPheSerPheThrLysTyrPheLeuLysIleGluLys

AACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCATCCTGGAGATAACA  240
AsnGlyLysValSerGlyThrLysLysGluAsnCysProTyrSerIleLeuGluIleThr

TCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCAACTATTACTTAGCCATG  300
SerValGluIleGlyValValAlaValLysAlaIleAsnSerAsnTyrTyrLeuAlaMet

AACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAG  360
AsnLysLysGlyLysLeuTyrGlySerLysGluPheAsnAsnAspCysLysLeuLysGlu

AGGATAGAGGAAAATGGATACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGG  420
ArgIleGluGluAsnGlyTyrAsnThrTyrAlaSerPheAsnTrpGlnHisAsnGlyArg

CAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGG  480
GlnMetTyrValAlaLeuAsnGlyLysGlyAlaProArgArgGlyGlnLysThrArgArg

AAAAACACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCATAG  525
LysAsnThrSerAlaHisPheLeuProMetValValHisSer *
```

FIG.24A

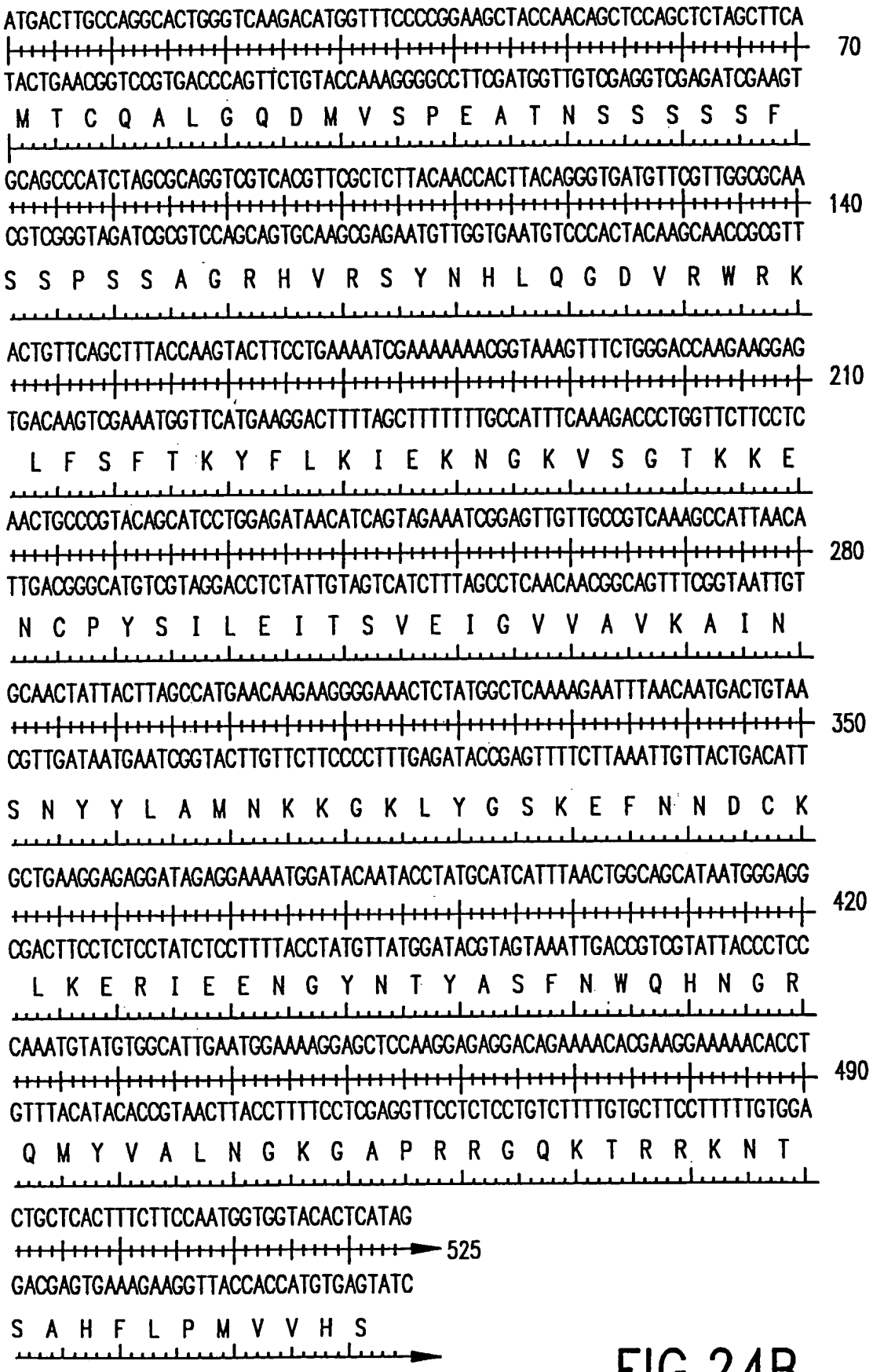

ATGACTTGCCAGGCACTGGGTCAAGACATGGTTTCCCCGGAAGCTACCAACAGCTCCAGCTCTAGCTTCA
70
TACTGAACGGTCCGTGACCCAGTTCTGTACCAAAGGGGCCTTCGATGGTTGTCGAGGTCGAGATCGAAGT
M T C Q A L G Q D M V S P E A T N S S S S S F
GCAGCCCATCTAGCGCAGGTCGTCACGTTCGCTCTTACAACCACTTACAGGGTGATGTTCGTTGGCGCAA
140
CGTCGGGTAGATCGCGTCCAGCAGTGCAAGCGAGAATGTTGGTGAATGTCCCACTACAAGCAACCGCGTT
S S P S S A G R H V R S Y N H L Q G D V R W R K
ACTGTTCAGCTTTACCAAGTACTTCCTGAAAATCGAAAAAAACGGTAAAGTTTCTGGGACCAAGAAGGAG
210
TGACAAGTCGAAATGGTTCATGAAGGACTTTTAGCTTTTTTTGCCATTTCAAAGACCCTGGTTCTTCCTC
L F S F T K Y F L K I E K N G K V S G T K K E
AACTGCCCGTACAGCATCCTGGAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACA
280
TTGACGGGCATGTCGTAGGACCTCTATTGTAGTCATCTTTAGCCTCAACAACGGCAGTTTCGGTAATTGT
N C P Y S I L E I T S V E I G V V A V K A I N
GCAACTATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAATGACTGTAA
350
CGTTGATAATGAATCGGTACTTGTTCTTCCCCTTTGAGATACCGAGTTTTCTTAAATTGTTACTGACATT
S N Y Y L A M N K K G K L Y G S K E F N N D C K
GCTGAAGGAGAGGATAGAGGAAAATGGATACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGG
420
CGACTTCCTCTCCTATCTCCTTTTACCTATGTTATGGATACGTAGTAAATTGACCGTCGTATTACCCTCC
L K E R I E E N G Y N T Y A S F N W Q H N G R
CAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGGAAAAACACCT
490
GTTTACATACACCGTAACTTACCTTTTCCTCGAGGTTCCTCTCCTGTCTTTTGTGCTTCCTTTTTGTGGA
Q M Y V A L N G K G A P R R G Q K T R R K N T
CTGCTCACTTTCTTCCAATGGTGGTACACTCATAG
525
GACGAGTGAAAGAAGGTTACCACCATGTGAGTATC
S A H F L P M V V H S

FIG.24B

ATGACCTGCCAGGCTCTGGGTCAGGACATGGTTTCTCCGGAAGCTACCAACTCTTCC
TCTTCCTCTTTCTCTTCCCCGTCTTCCGCTGGTCGTCACGTTCGTTCTTACAACCAC
CTGCAGGGTGACGTTCGTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAA
ATCGAAAAAAAACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCATC
CTGGAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCAAC
TATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAAT
GACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGATACAATACCTATGCATCATTT
AACTGGCAGCATAATGGGAGGCAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCA
AGGAGAGGACAGAAAACACGAAGGAAAAACACCTCTGCTCACTTTCTTCCAATGGTG
GTACACTCATAG

MTCQALGQDMVSPEATNSSSSSFSSPSSAGRHVRSYNHLQGDVRWRKLFSFTKYFLKIE
KNGKVSGTKKENCPYSILEITSVEIGVVAVKAINSNYYLAMNKKGKLYGSKEFNNDCKL
KERIEENGYNTYASFNWQHNGRQMYVALNGKGAPRRGQKTRRKNTSAHFLPMVVHS.

FIG.25

ATGGCTGGTCGTCACGTTCGTTCTTACAACCACCTGCAGGGTGACGTTCGTTGGCGT
AAACTGTTCTCTTTCACCAAATACTTCCTGAAAATCGAAAAAAACGGTAAAGTTTCT
GGGACCAAGAAGGAGAACTGCCCGTACAGCATCCTGGAGATAACATCAGTAGAAATC
GGAGTTGTTGCCGTCAAAGCCATTAACAGCAACTATTACTTAGCCATGAACAAGAAG
GGGAAACTCTATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAGAGGATA
GAGGAAAATGGATACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGGCAA
ATGTATGTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGG
AAAAACACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCATAG

MAGRHVRSYNHLQGDVRWRKLFSFTKYFLKIEKNGKVSGTKKENCPYSILEITSVEIGV
VAVKAINSNYYLAMNKKGKLYGSKEFNNDCKLKERIEENGYNTYASFNWQHNGRQMYVA
LNGKGAPRRGQKTRRKNTSAHFLPMVVHS.

FIG.26

ATGGTTCGTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAAATCGAAAAA
AACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCATCCTGGAGATA
ACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCAACTATTACTTA
GCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAATGACTGTAAG
CTGAAGGAGAGGATAGAGGAAAATGGATACAATACCTATGCATCATTTAACTGGCAG
CATAATGGGAGGCAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGA
CAGAAAACACGAAGGAAAAACACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCA
TAG

MVRWRKLFSFTKYFLKIEKNGKVSGTKKENCPYSILEITSVEIGVVAVKAINSNYYLAM
NKKGKLYGSKEFNNDCKLKERIEENGYNTYASFNWQHNGRQMYVALNGKGAPRRGQKTR
RKNTSAHFLPMVVHS.

FIG.27

ATGGAAAAAAACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCAT
CCTGGAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCA
ACTATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAAC
AATGACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGATACAATACCTATGCATC
ATTTAACTGGCAGCATAATGGGAGGCAAATGTATGTGGCATTGAATGGAAAAGGAG
CTCCAAGGAGAGGACAGAAAACACGAAGGAAAAACACCTCTGCTCACTTTCTTCCA
ATGGTGGTACACTCATAG

MEKNGKVSGTKKENCPYSILEITSVEIGVVAVKAINSNYYLAMNKKGKLYGSKEFNNDC
KLKERIEENGYNTYASFNWQHNGRQMYVALNGKGAPRRGQKTRRKNTSAHFLPMVVH
S.

FIG.28

ATGGAGAACTGCCCGTACAGCATCCTGGAGATAACATCAGTAGAAATCGGAGTTGT
TGCCGTCAAAGCCATTAACAGCAACTATTACTTAGCCATGAACAAGAAGGGGAAAC
TCTATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAGAGGATAGAGGAA
AATGGATACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGGCAAATGTA
TGTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGGAAAA
ACACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCATAG

MENCPYSILEITSVEIGVVAVKAINSNYYLAMNKKGKLYGSKEFNNDCKLKERIEENGY
NTYASFNWQHNGRQMYVALNGKGAPRRGQKTRRKNTSAHFLPMVVHS.

FIG.29

ATGGTCAAAGCCATTAACAGCAACTATTACTTAGCCATGAACAAGAAGGGGAAACT
CTATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAGAGGATAGAGGAAA
ATGGATACAATACCTATGCATCATTTAACTGGCAGCATAATGGGAGGCAAATGTAT
GTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACACGAAGGAAAAA
CACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCATAG

MVKAINSNYYLAMNKKGKLYGSKEFNNDCKLKERIEENGYNTYASFNWQHNGRQMY
VALNGKGAPRRGQKTRRKNTSAHFLPMVVHS.

FIG.30

ATGGGGAAACTCTATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAGGAGAG
GATAGAGGAAAATGGATACAATACCTATGCATCATTTAACTGGCAGCATAATGGGA
GGCAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCAAGGAGAGGACAGAAAACA
CGAAGGAAAAACACCTCTGCTCACTTTCTTCCAATGGTGGTACACTCATAG

MGKLYGSKEFNNDCKLKERIEENGYNTYASFNWQHNGRQMYVALNGKGAPRRGQKT
RRKNTSAHFLPMVVHS.

FIG.31

ATGACCTGCCAGGCTCTGGGTCAGGACATGGTTTCTCCGGAAGCTACCAACTCTTCC
TCTTCCTCTTTCTCTTCCCCGTCTTCCGCTGGTCGTCACGTTCGTTCTTACAACCAC
CTGCAGGGTGACGTTCGTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAA
ATCGAAAAAAAACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCATC
CTGGAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCAAC
TATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAAT
GACTGTAAGCTGAAG

MTCQALGQDMVSPEATNSSSSSFSSPSSAGRHVRSYNHLQGDVRWRKLFSFTKYFLKIE
KNGKVSGTKKENCPYSILEITSVEIGVVAVKAINSNYYLAMNKKGKLYGSKEFNNDCKL
K

FIG.32

ATGGCTGGTCGTCACGTTCGTTCTTACAACCACCTGCAGGGTGACGTTCGTTGGCGT
AAACTGTTCTCTTTCACCAAATACTTCCTGAAAATCGAAAAAAAACGGTAAAGTTTCT
GGGACCAAGAAGGAGAACTGCCCGTACAGCATCCTGGAGATAACATCAGTAGAAATC
GGAGTTGTTGCCGTCAAAGCCATTAACAGCAACTATTACTTAGCCATGAACAAGAAG
GGGAAACTCTATGGCTCAAAAGAATTTAACAATGACTGTAAGCTGAAG

MAGRHVRSYNHLQGDVRWRKLFSFTKYFLKIEKNGKVSGTKKENCPYSILEITSVEIGV
VAVKAINSNYYLAMNKKGKLYGSKEFNNDCKLK

FIG.33

C-37 To Ser

ATGACCTCTCAGGCTCTGGGTCAGGACATGGTTTCTCCGGAAGCTACCAACTCTTCC
TCTTCCTCTTTCTCTTCCCCGTCTTCCGCTGGTCGTCACGTTCGTTCTTACAACCAC
CTGCAGGGTGACGTTCGTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAA
ATCGAAAAAAACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTGCCCGTACAGCATC
CTGGAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCAAC
TATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAAT
GACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGATACAATACCTATGCATCATTT
AACTGGCAGCATAATGGGAGGCAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCA
AGGAGAGGACAGAAAACACGAAGGAAAAACACCTCTGCTCACTTTCTTCCAATGGTG
GTACACTCATAG

FIG.34

C-106 To Ser

ATGACCTGCCAGGCTCTGGGTCAGGACATGGTTTCTCCGGAAGCTACCAACTCTTCC
TCTTCCTCTTTCTCTTCCCCGTCTTCCGCTGGTCGTCACGTTCGTTCTTACAACCAC
CTGCAGGGTGACGTTCGTTGGCGTAAACTGTTCTCTTTCACCAAATACTTCCTGAAA
ATCGAAAAAAACGGTAAAGTTTCTGGGACCAAGAAGGAGAACTCTCCGTACAGCATC
CTGGAGATAACATCAGTAGAAATCGGAGTTGTTGCCGTCAAAGCCATTAACAGCAAC
TATTACTTAGCCATGAACAAGAAGGGGAAACTCTATGGCTCAAAAGAATTTAACAAT
GACTGTAAGCTGAAGGAGAGGATAGAGGAAAATGGATACAATACCTATGCATCATTT
AACTGGCAGCATAATGGGAGGCAAATGTATGTGGCATTGAATGGAAAAGGAGCTCCA
AGGAGAGGACAGAAAACACGAAGGAAAAACACCTCTGCTCACTTTCTTCCAATGGTG
GTACACTCATAG

FIG.35

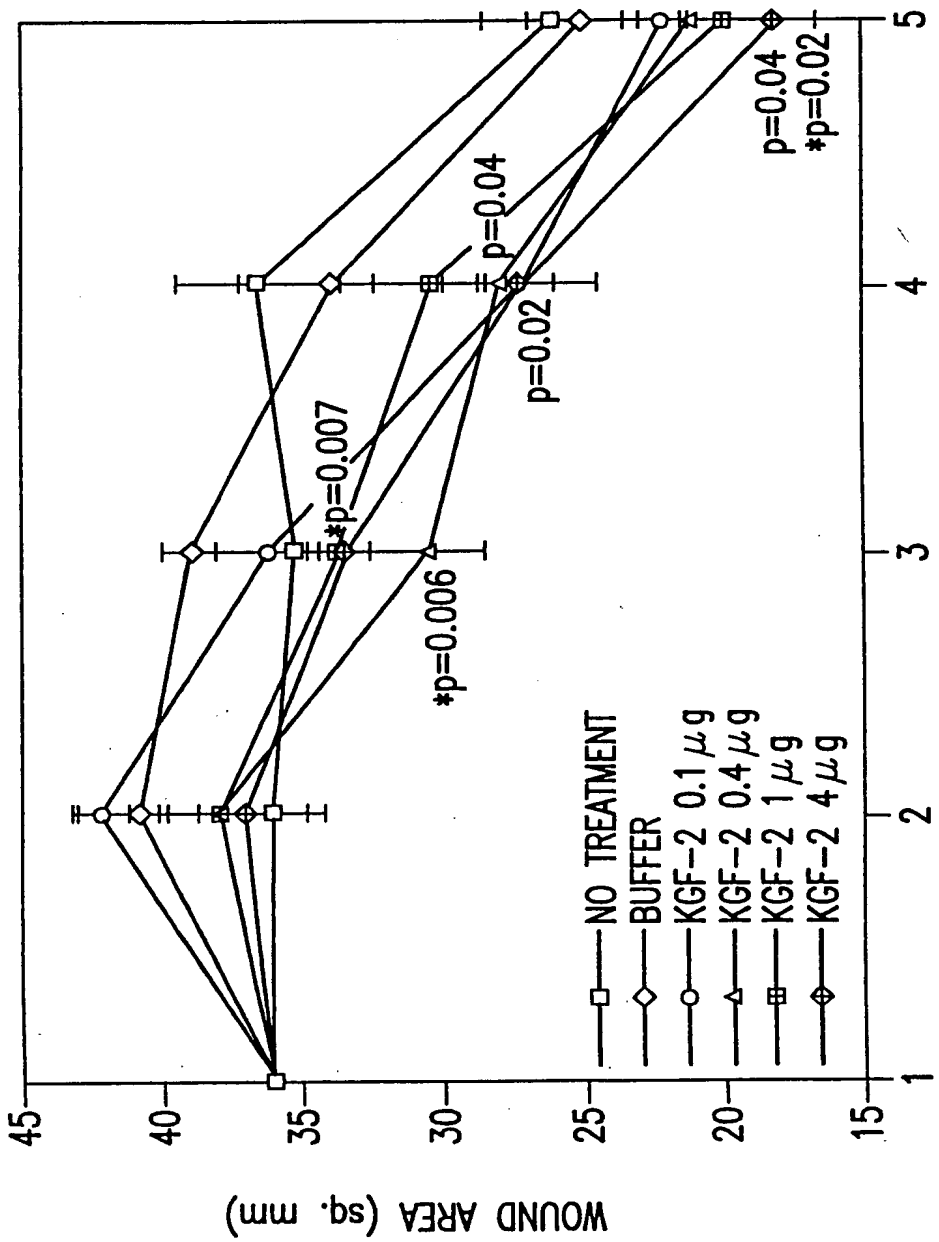

WOUND AREA (sq. mm)
45
40
35
30
25
20
15
1
2
3
4
5
DAYS POST-WOUNDING
NO TREATMENT
BUFFER
KGF-2 0.1 μg
KGF-2 0.4 μg
KGF-2 1 μg
KGF-2 4 μg
*p=0.006
*p=0.007
p=0.02
p=0.04
p=0.04
*p=0.02

FIG.36

EFFECT OF KGF-2 Δ33 ON NORMAL WOUND HEALING RAT MODEL

TREATMENT GROUPS	WOUND SIZE (mm)	% WOUND CLOSURE	HISTOLOGICAL SCORE	RE-EPITH. (μm)	BrdU SCORE
NO TREATMENT	25.9±2.5	58.8±3.7	6.8±0.2	1142±141	3.8±0.4
BUFFER	25.1±1.7	60.2±2.6	6.4±0.2	923±61	5.0±0.4
KGF-2/Δ33 (0.1μg)	22.0±0.9	65±1.4	6.8±0.2	1275±148	4.6±0.7
KGF-2/Δ33 (0.4 μg)	21.1±1.4	68.4±2.4	8.0±0.5 p=0.0445*	1310±182	4.2±0.7
KGF-2/Δ33 (1.0 μg)	19.9±1.5	66.2±2.1	8.4±0.4 p=0.0159* p=0.0053†	1389±115 p=0.0074†	3.3±0.25 p=0.0217†
KGF-2/Δ33 (4.0μg)	18.1±1.6 p=0.0398* p=0.0200†	71.2±2.6 p=0.0367* p=0.0217†	8.5±0.3 p=0.0047* p=0.0445†	1220±89 p=0.0254†	5.3±0.9

FIG.37

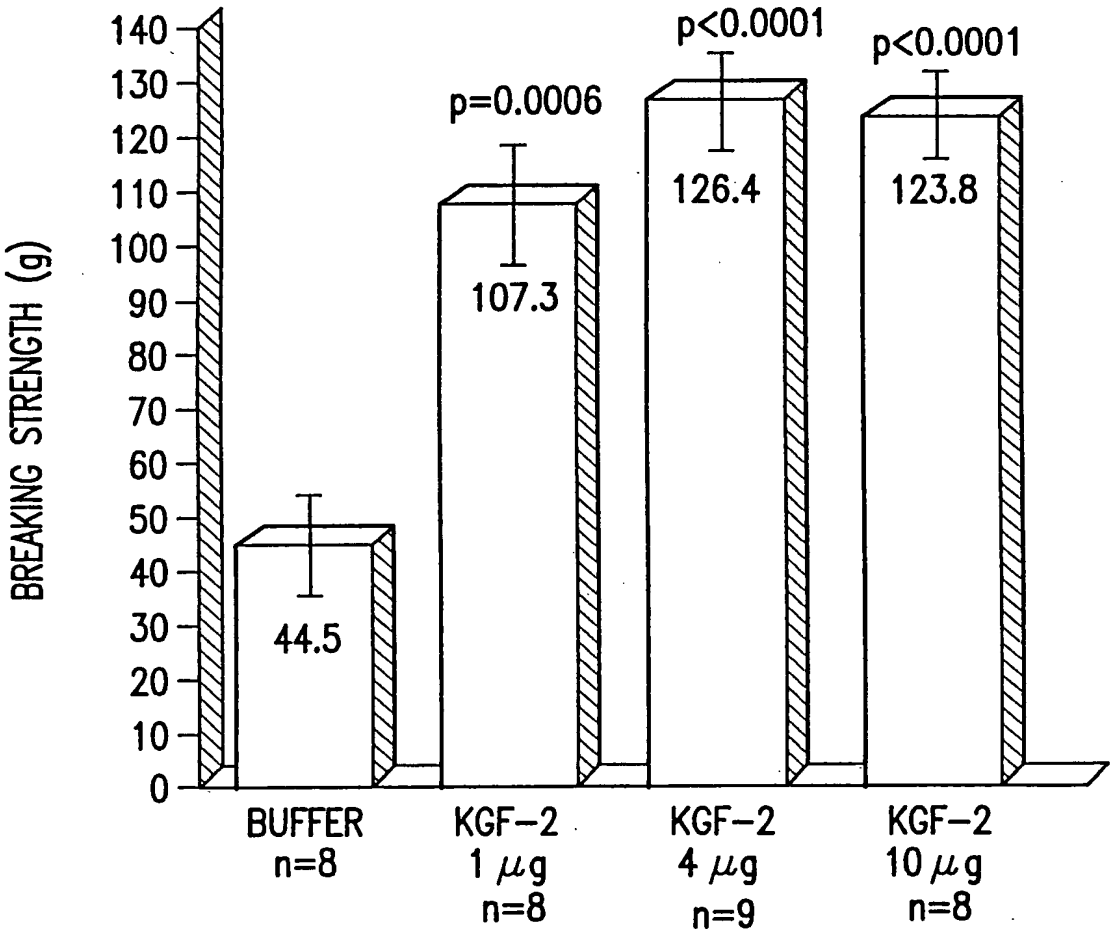

BREAKING STRENGTH (g)
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
44.5
107.3
p=0.0006
126.4
p<0.0001
123.8
p<0.0001
BUFFER
n=8
KGF-2
1 μg
n=8
KGF-2
4 μg
n=9
KGF-2
10 μg
n=8

FIG.38

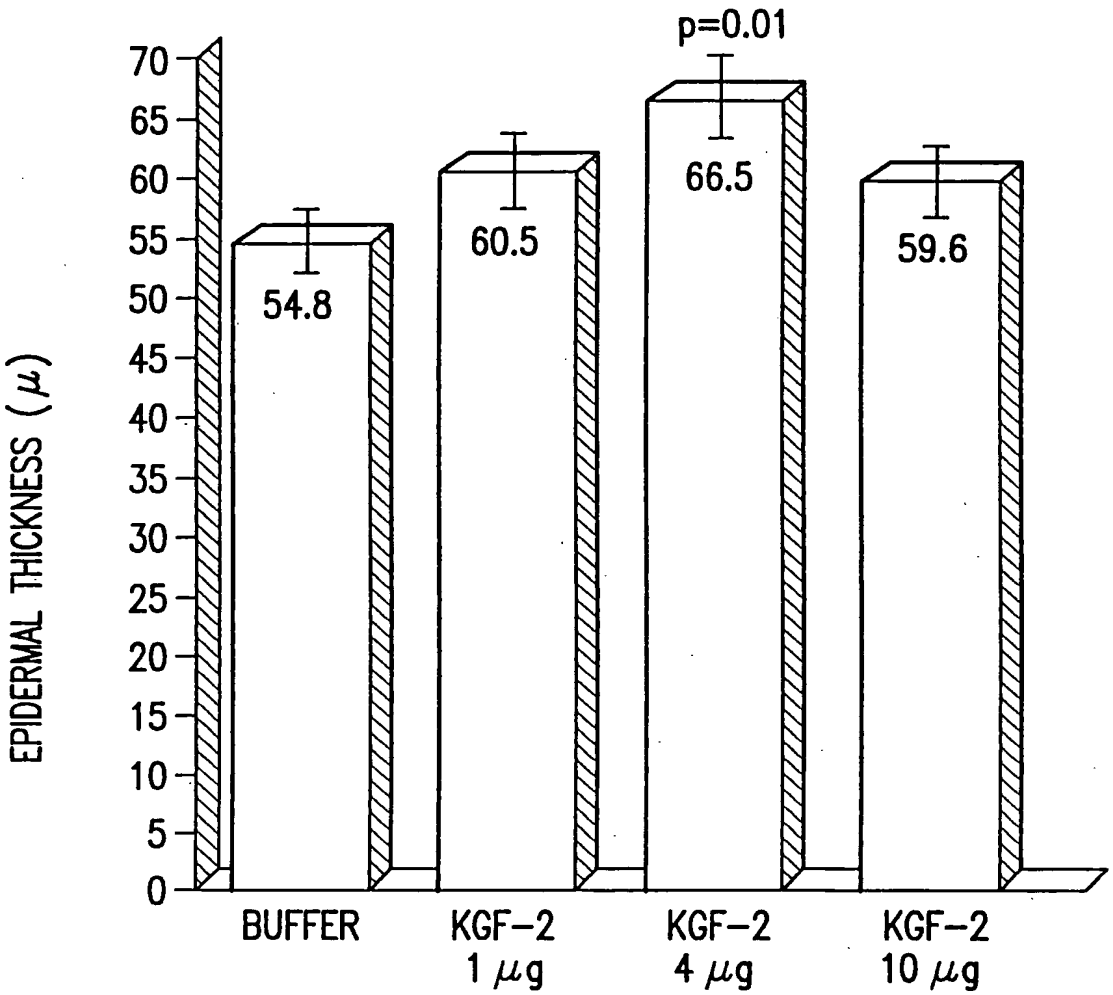

p=0.01
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
EPIDERMAL THICKNESS (μ)
54.8
60.5
66.5
59.6
BUFFER
KGF-2
1 μg
KGF-2
4 μg
KGF-2
10 μg

FIG.39

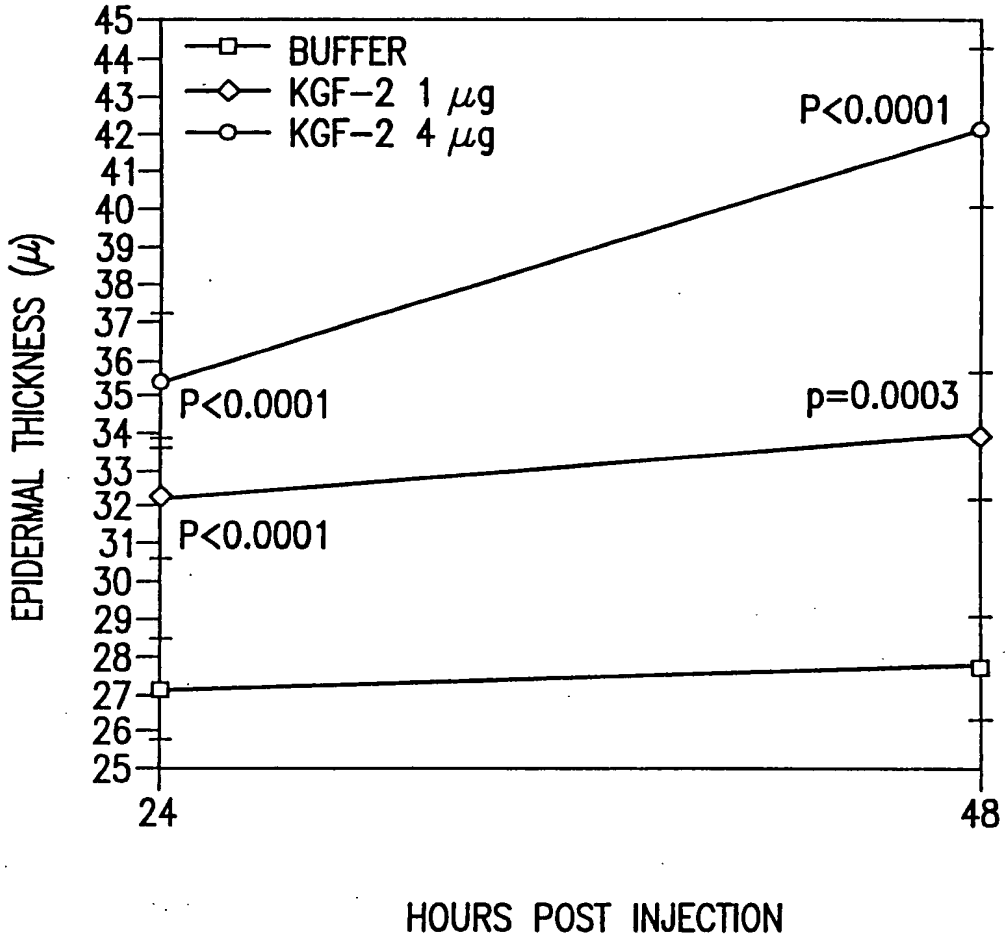

BUFFER
KGF-2 1 μg
KGF-2 4 μg
P<0.0001
P<0.0001
p=0.0003
P<0.0001
EPIDERMAL THICKNESS (μ)
45
44
43
42
41
40
39
38
37
36
35
34
33
32
31
30
29
28
27
26
25
24
48
HOURS POST INJECTION

FIG.40

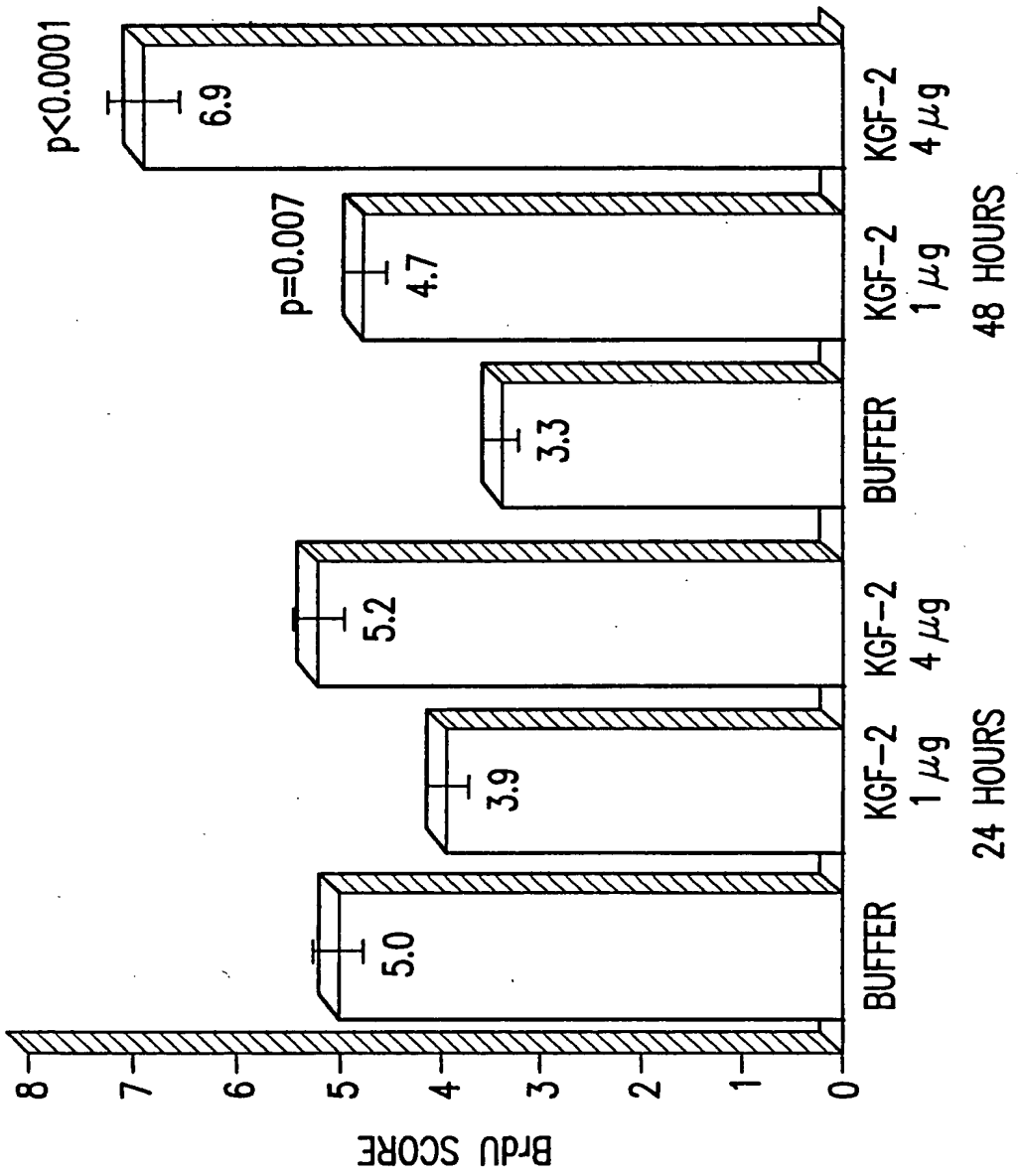

BrdU SCORE
0
1
2
3
4
5
6
7
8
5.0
3.9
5.2
3.3
4.7
6.9
p=0.007
p<0.0001
BUFFER
KGF-2 1 μg
KGF-2 4 μg
BUFFER
KGF-2 1 μg
KGF-2 4 μg
24 HOURS
48 HOURS

FIG.41

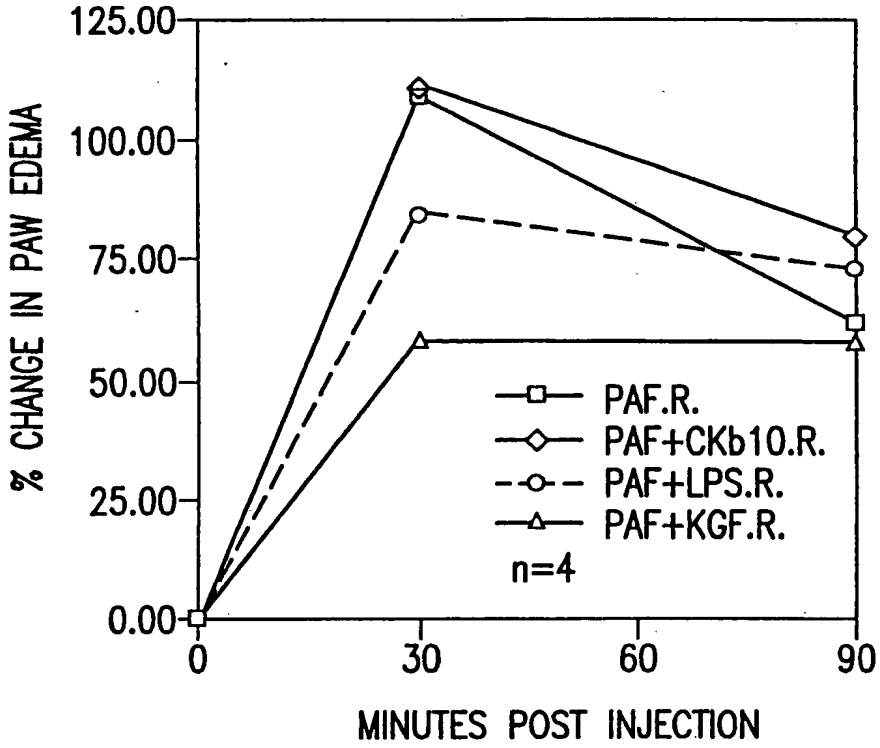


FIG.42A

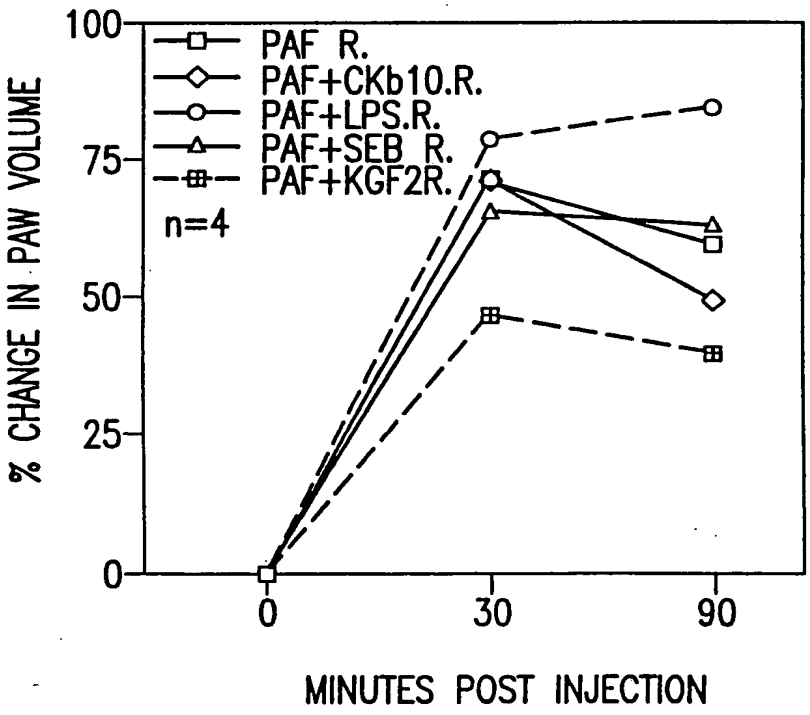


FIG.42B

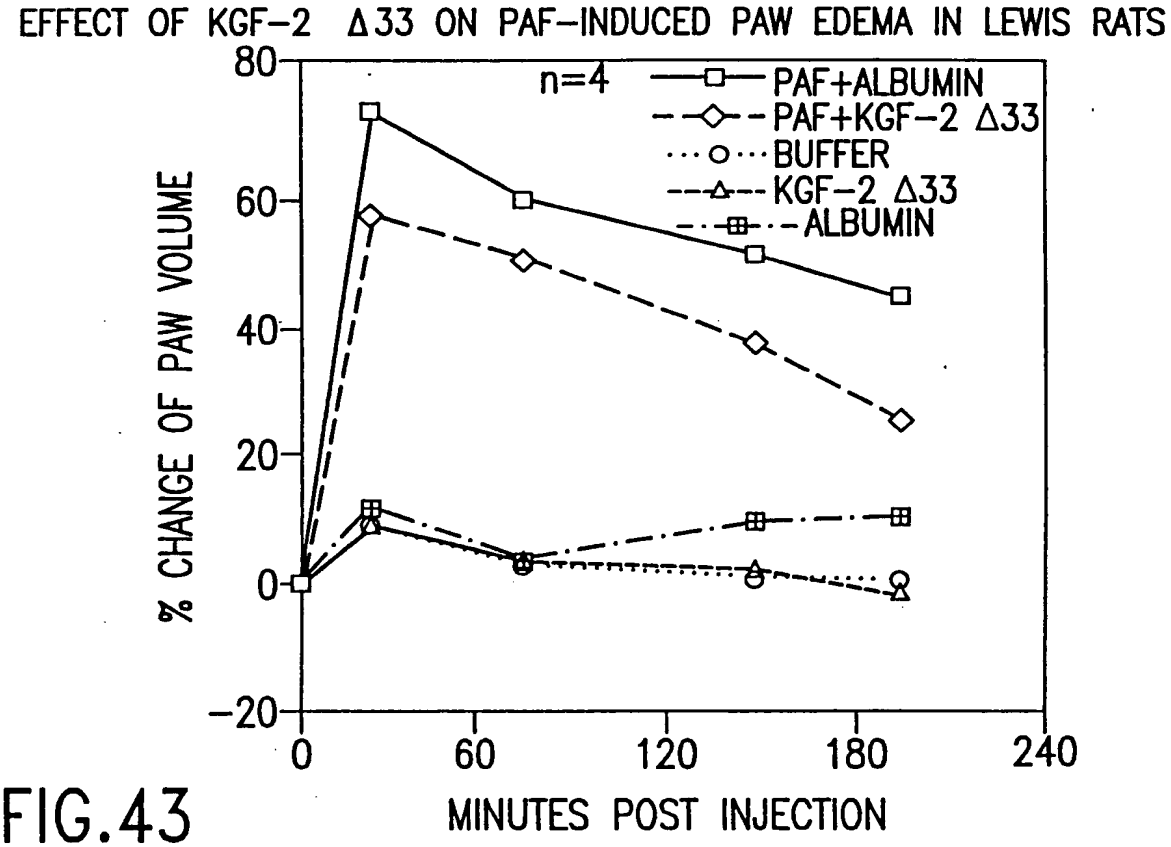

EFFECT OF KGF-2 Δ33 ON PAF-INDUCED PAW EDEMA IN LEWIS RATS
n=4
PAF+ALBUMIN
PAF+KGF-2 Δ33
BUFFER
KGF-2 Δ33
ALBUMIN
% CHANGE OF PAW VOLUME
80
60
40
20
0
-20
0
60
120
180
240
MINUTES POST INJECTION

FIG.43

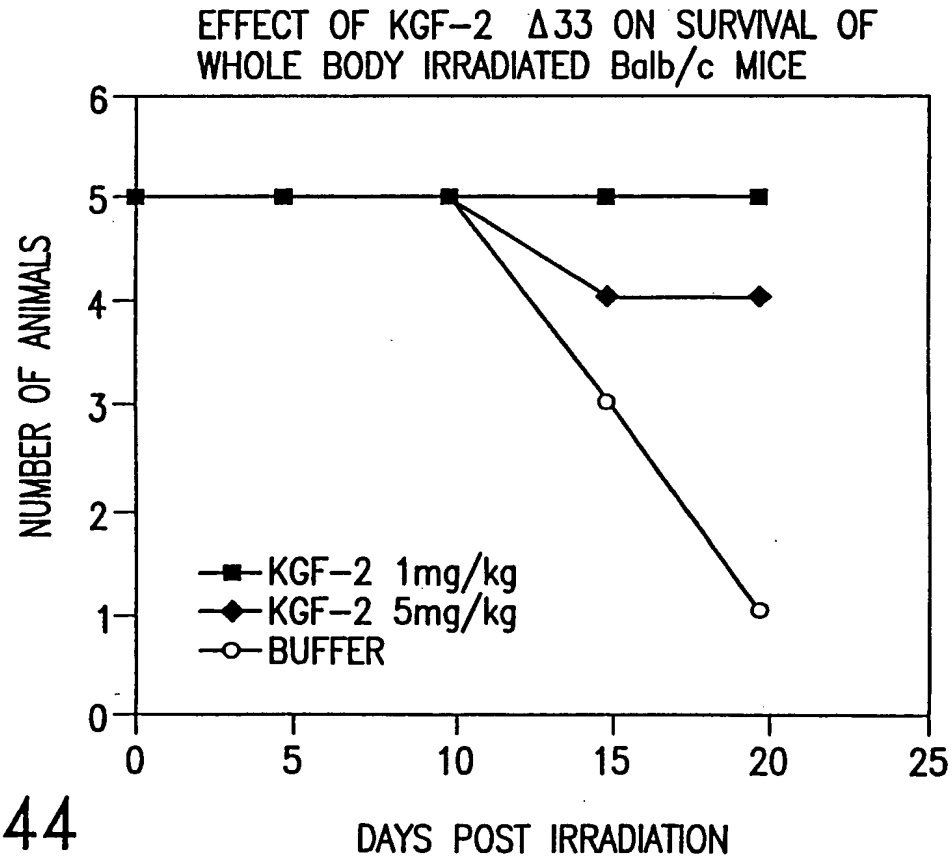

EFFECT OF KGF-2 Δ33 ON SURVIVAL OF WHOLE BODY IRRADIATED Balb/c MICE
NUMBER OF ANIMALS
6
5
4
3
2
1
0
KGF-2 1mg/kg
KGF-2 5mg/kg
BUFFER
0
5
10
15
20
25
DAYS POST IRRADIATION

FIG.44

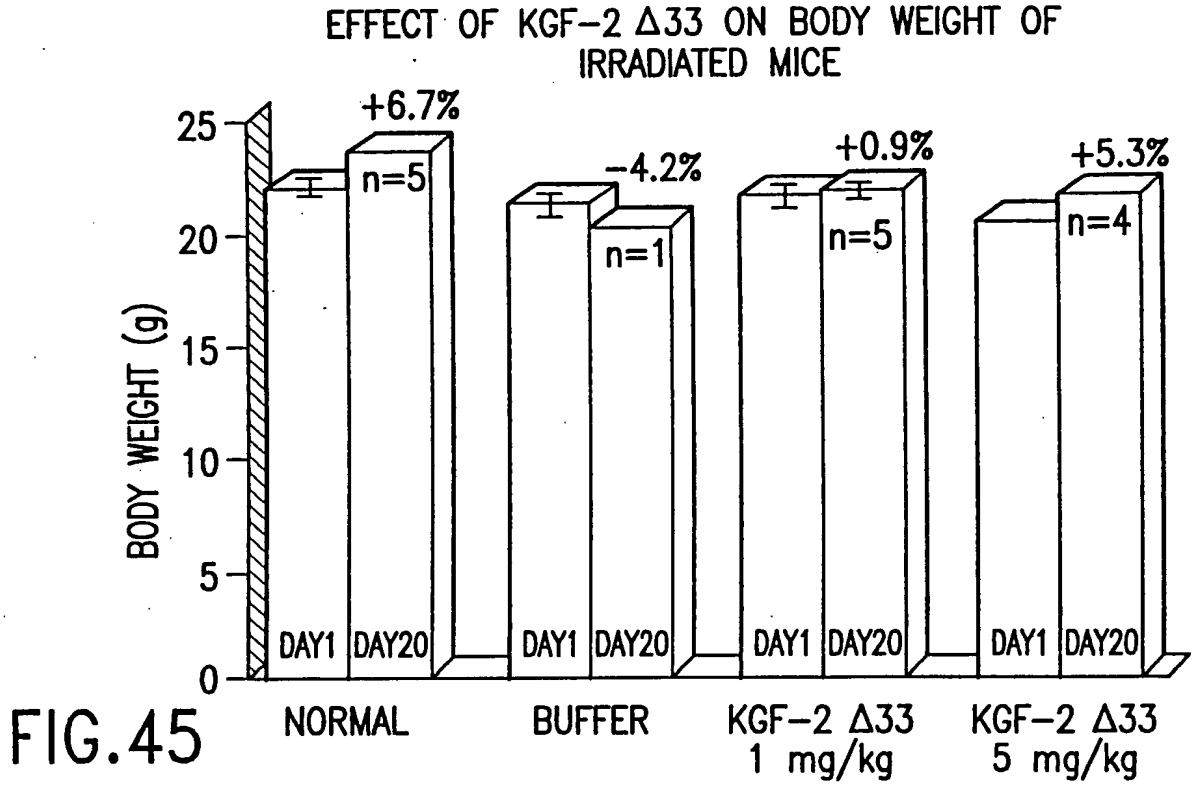

EFFECT OF KGF-2 Δ33 ON BODY WEIGHT OF IRRADIATED MICE
BODY WEIGHT (g)
25
20
15
10
5
0
+6.7%
n=5
-4.2%
n=1
+0.9%
n=5
+5.3%
n=4
DAY1
DAY20
NORMAL
BUFFER
KGF-2 Δ33 1 mg/kg
KGF-2 Δ33 5 mg/kg

FIG.45

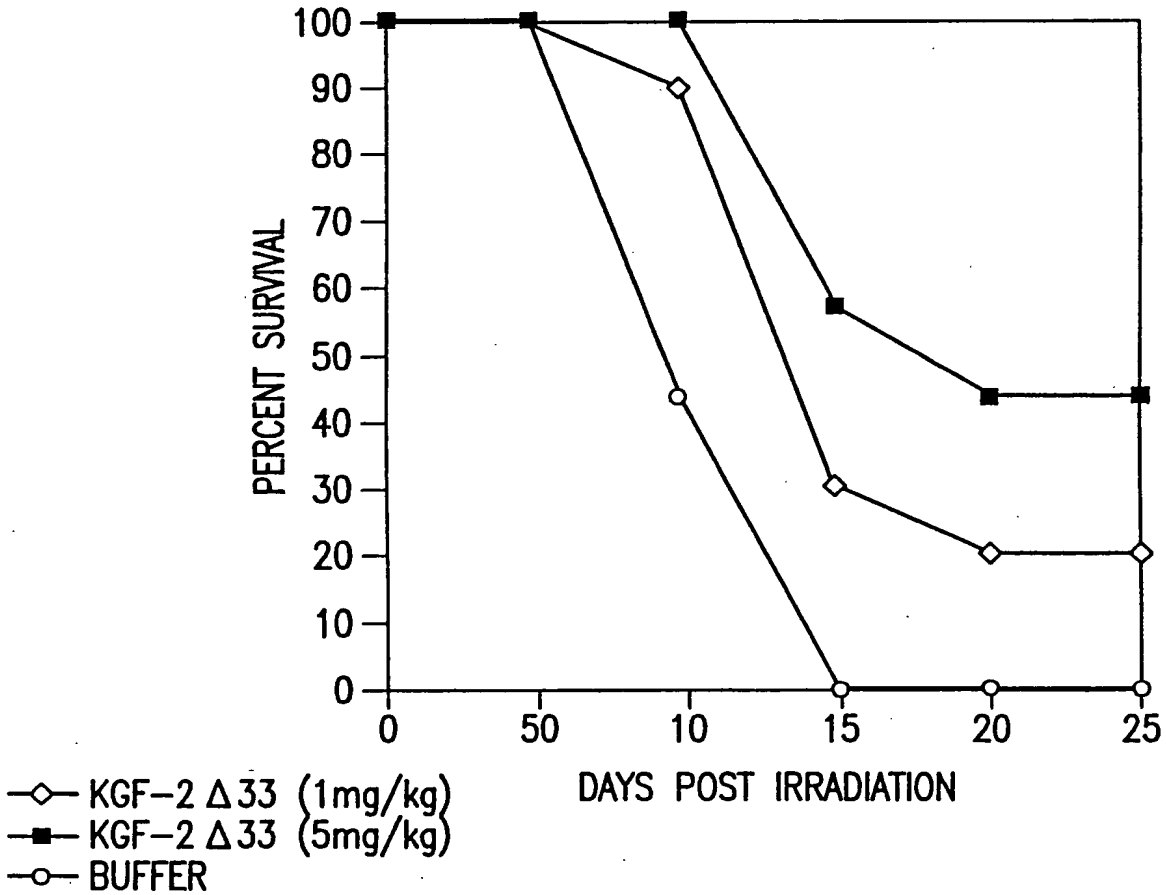

PERCENT SURVIVAL
100
90
80
70
60
50
40
30
20
10
0
0
50
10
15
20
25
DAYS POST IRRADIATION
KGF-2 Δ33 (1mg/kg)
KGF-2 Δ33 (5mg/kg)
BUFFER

FIG.46

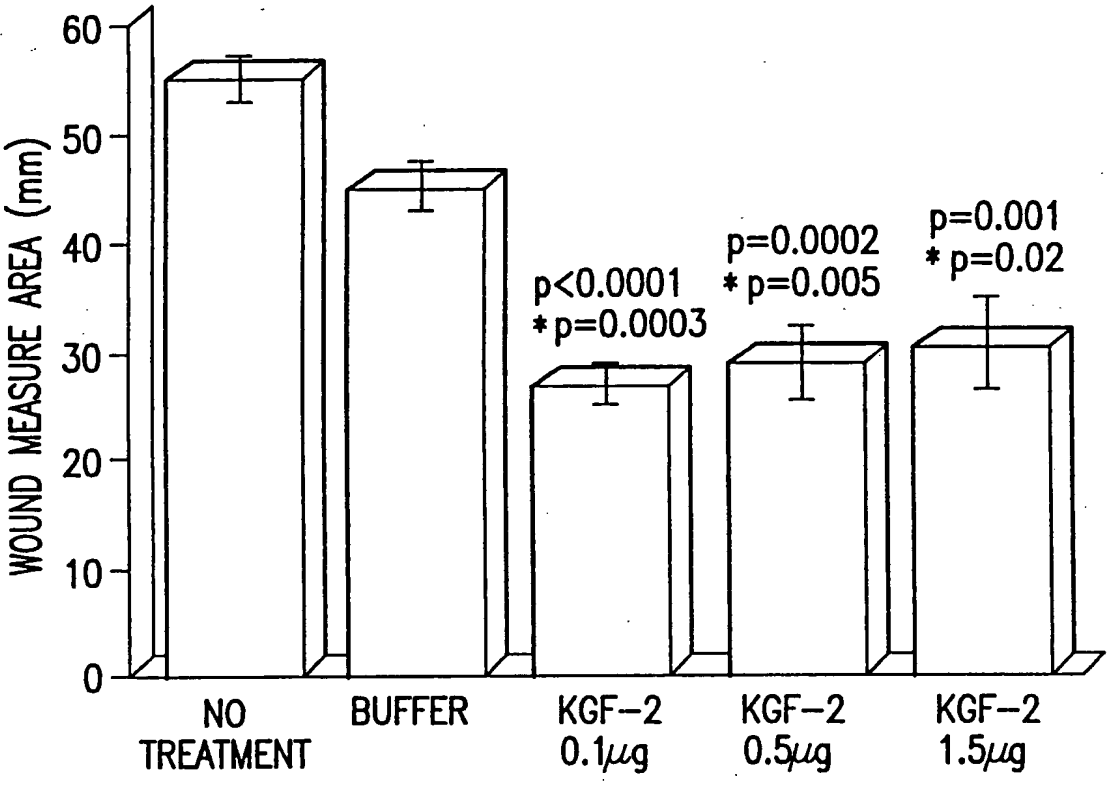

WOUND MEASURE AREA (mm)
60
50
40
30
20
10
0
p<0.0001
*p=0.0003
p=0.0002
*p=0.005
p=0.001
*p=0.02
NO TREATMENT
BUFFER
KGF-2 0.1μg
KGF-2 0.5μg
KGF-2 1.5μg
DAY 8 POSTWOUNDING

FIG.47

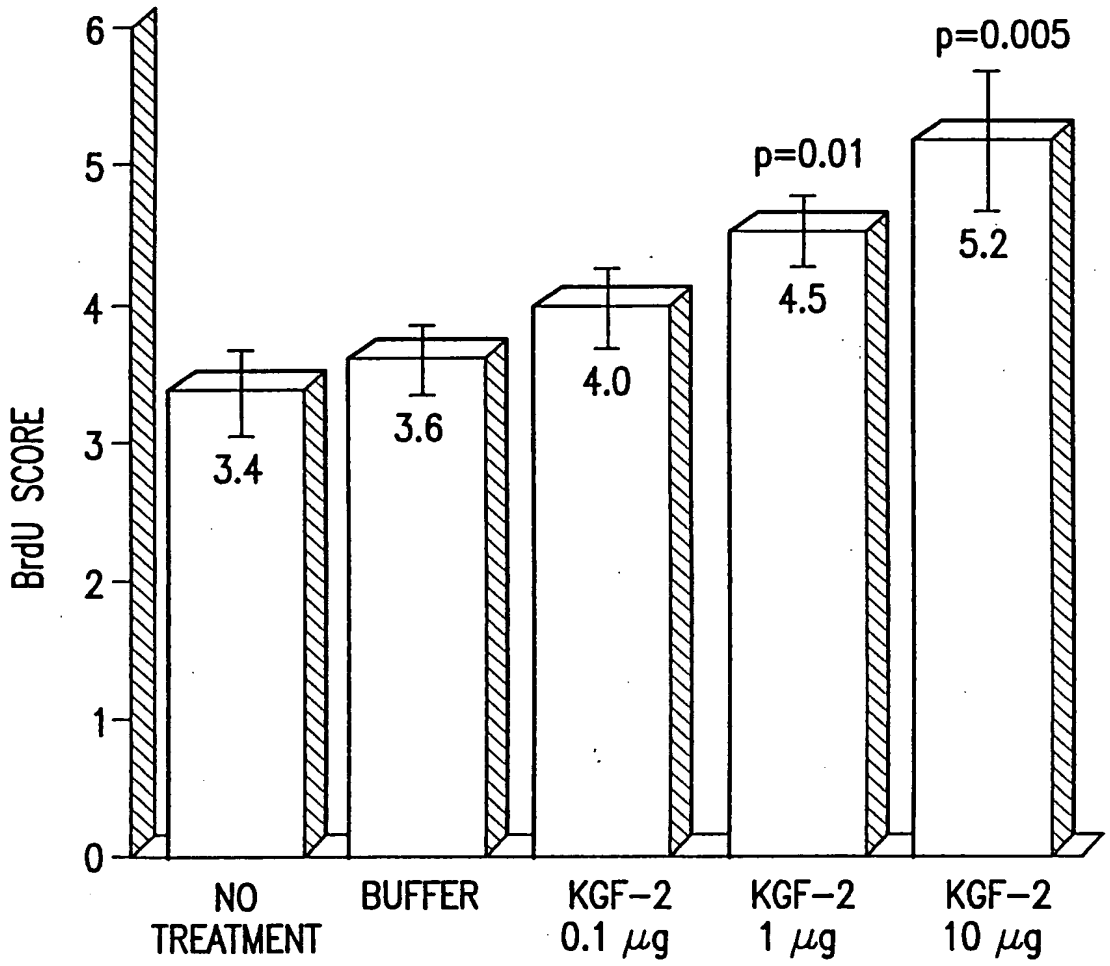

BrdU SCORE
0
1
2
3
4
5
6
3.4
3.6
4.0
4.5
5.2
p=0.01
p=0.005
NO TREATMENT
BUFFER
KGF-2 0.1 μg
KGF-2 1 μg
KGF-2 10 μg

FIG.48

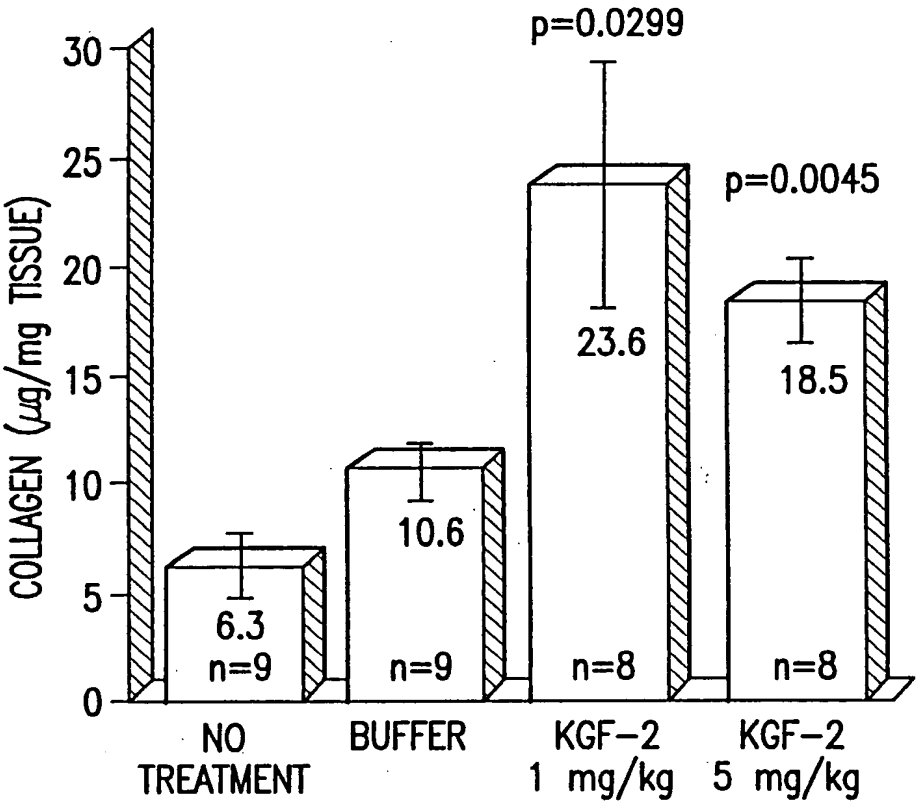

p=0.0299
p=0.0045
30
25
20
15
10
5
0
COLLAGEN (μg/mg TISSUE)
23.6
18.5
10.6
6.3
n=9
n=9
n=8
n=8
NO TREATMENT
BUFFER
KGF-2 1 mg/kg
KGF-2 5 mg/kg

FIG.49

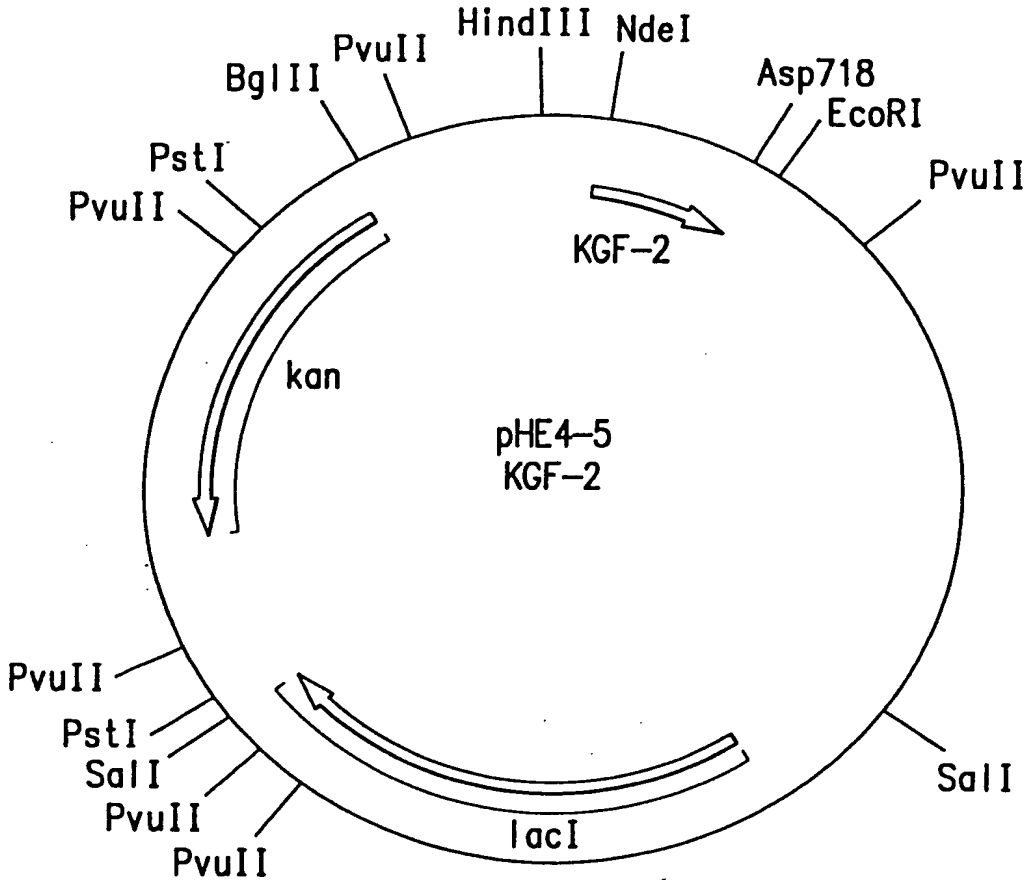

HindIII
NdeI
PvuII
BglII
Asp718
EcoRI
PstI
PvuII
PvuII
KGF-2
kan
pHE4-5
KGF-2
PvuII
PstI
SalI
PvuII
PvuII
lacI
SalI

FIG. 50

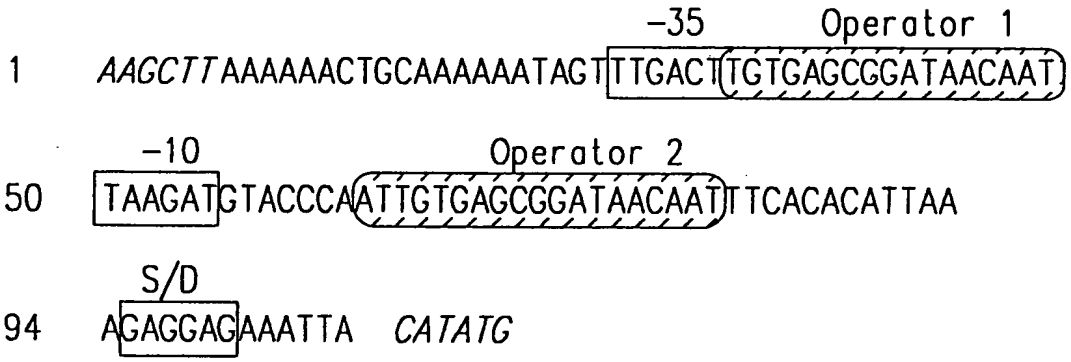

-35
Operator 1
1 AAGCTTAAAAAACTGCAAAAAATAGTTTGACTTGTGAGCGGATAACAAT
-10
Operator 2
50 TAAGATGTACCCAATTGTGAGCGGATAACAATTTCACACATTAA
S/D
94 AGAGGAGAAATTA CATATG

FIG. 51

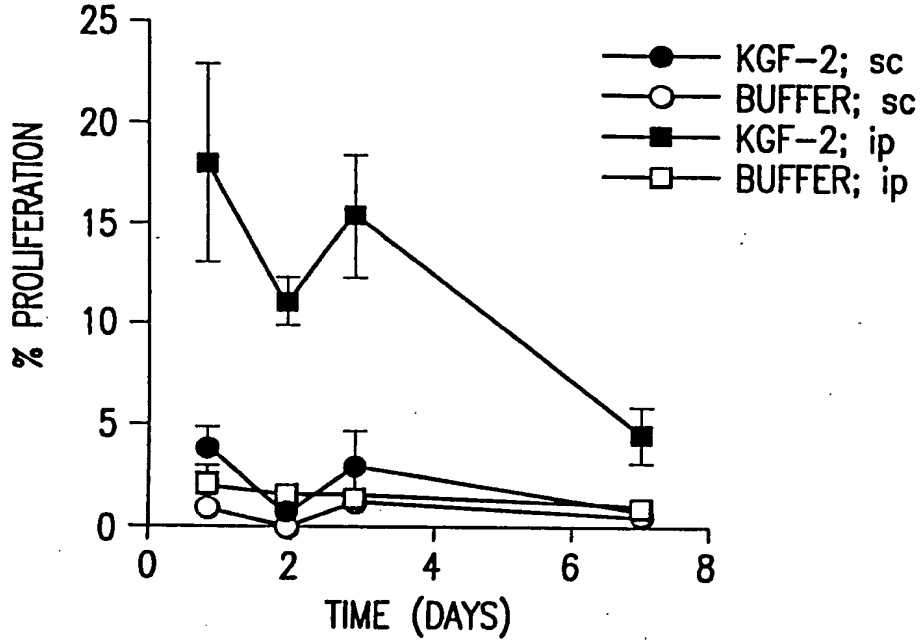

25
20
15
10
5
0
% PROLIFERATION
0
2
4
6
8
TIME (DAYS)
KGF-2; sc
BUFFER; sc
KGF-2; ip
BUFFER; ip

FIG. 52

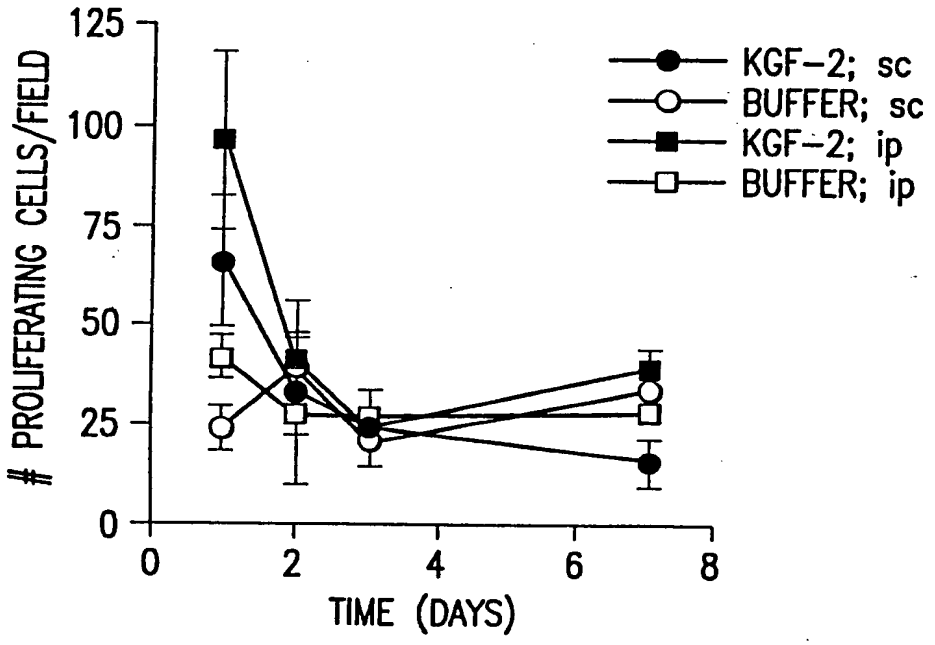

125
100
75
50
25
0
PROLIFERATING CELLS/FIELD
0
2
4
6
8
TIME (DAYS)
KGF-2; sc
BUFFER; sc
KGF-2; ip
BUFFER; ip

FIG. 53

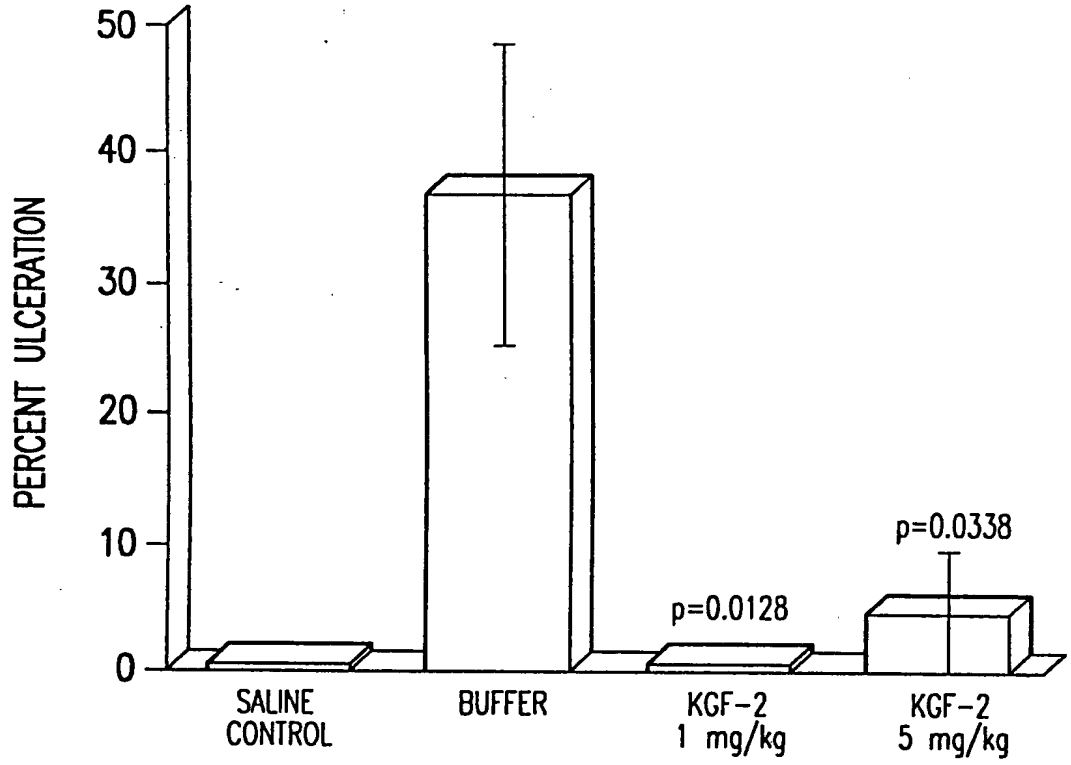

PERCENT ULCERATION
50
40
30
20
10
0
p=0.0338
p=0.0128
SALINE CONTROL
BUFFER
KGF-2 1 mg/kg
KGF-2 5 mg/kg

FIG. 54

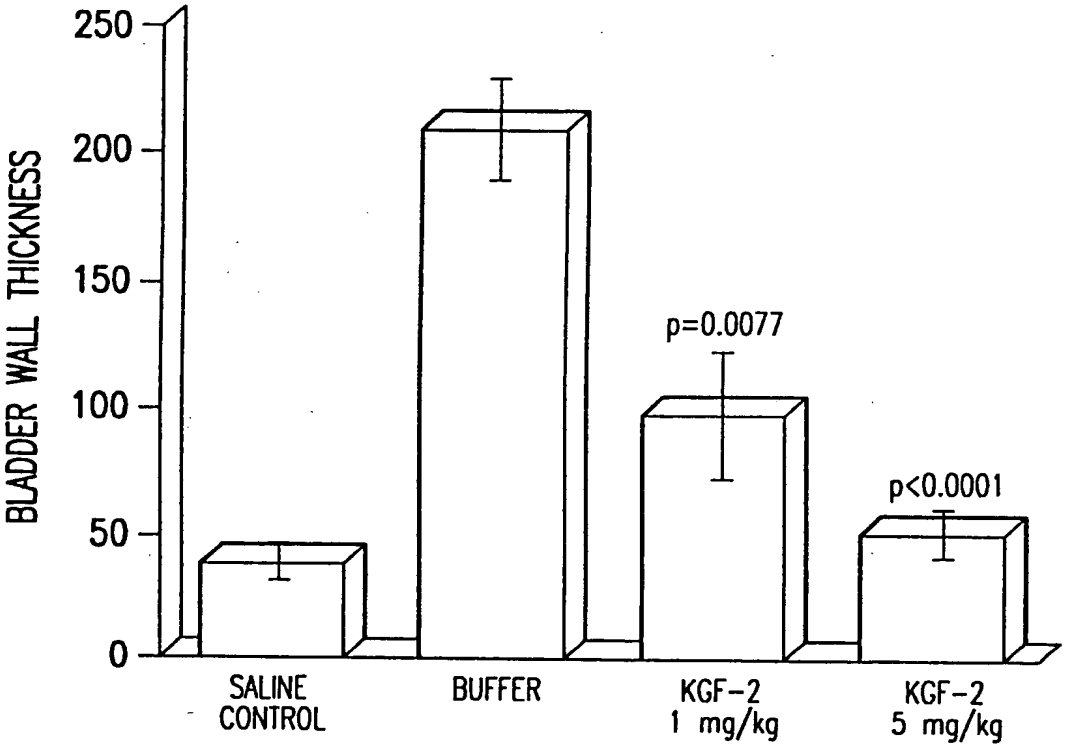

BLADDER WALL THICKNESS
250
200
150
100
50
0
p=0.0077
p<0.0001
SALINE CONTROL
BUFFER
KGF-2 1 mg/kg
KGF-2 5 mg/kg

FIG. 55

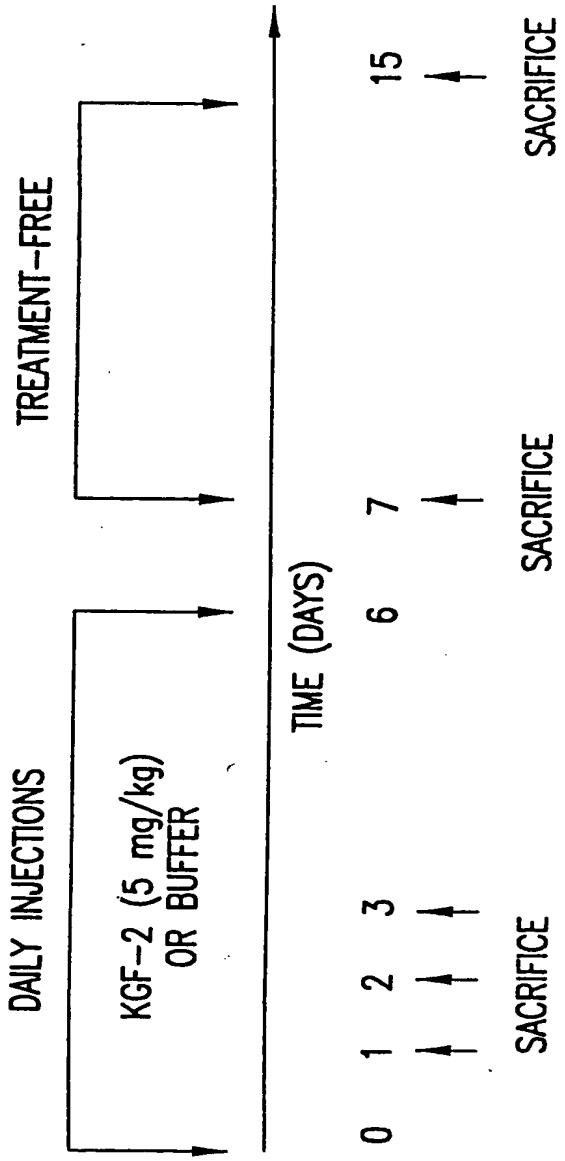

DAILY INJECTIONS
KGF-2 (5 mg/kg)
OR BUFFER
TREATMENT-FREE
TIME (DAYS)
0
1
2
3
6
7
15
SACRIFICE
SACRIFICE
SACRIFICE

FIG. 56

PROLIFERATION OF HEPATOCYTES FOLLOWING SYSTEMIC ADMINISTRATION OF KGF-2

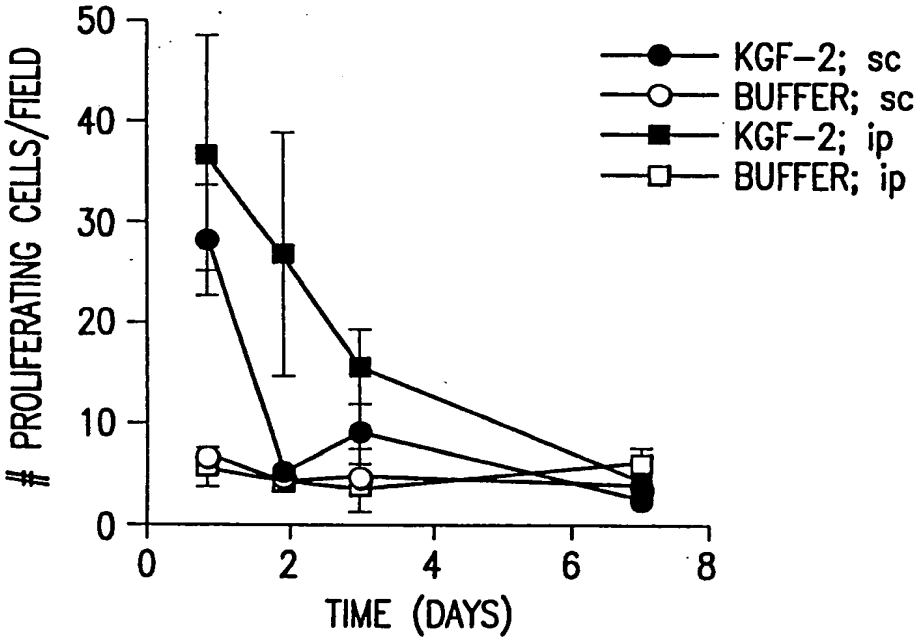


FIG. 57

PROLIFERATION OF PANCREATIC CELLS FOLLOWING SYSTEMIC ADMINISTRATION OF KGF-2

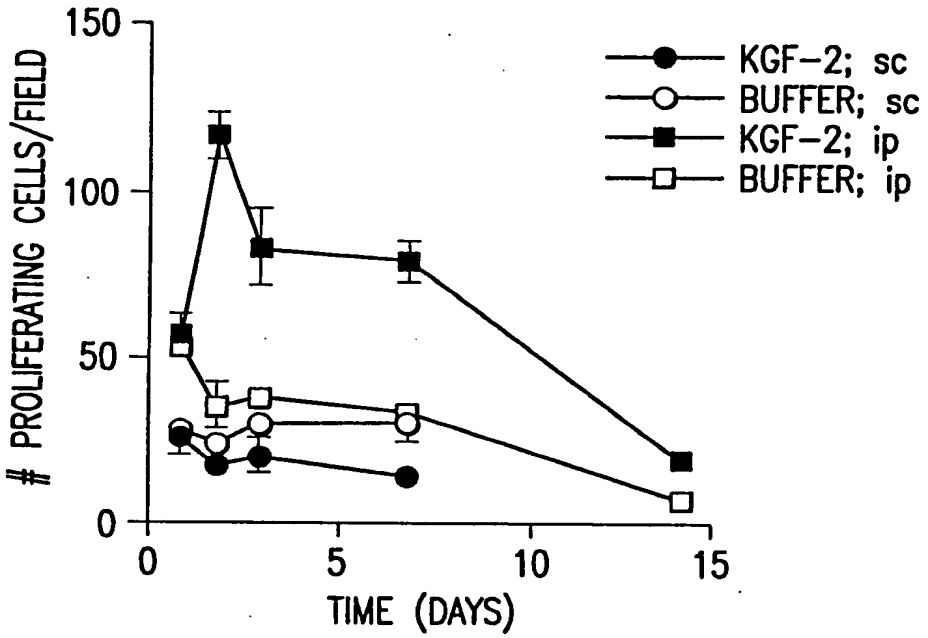


FIG. 58

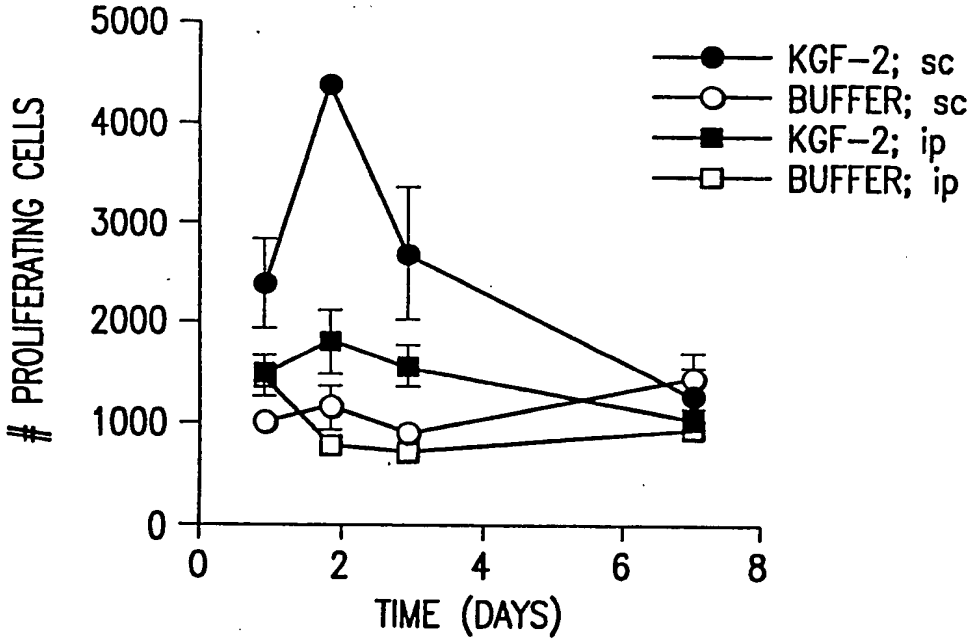

5000
4000
3000
2000
1000
0
PROLIFERATING CELLS
0
2
4
6
8
TIME (DAYS)
KGF-2; sc
BUFFER; sc
KGF-2; ip
BUFFER; ip

FIG. 59

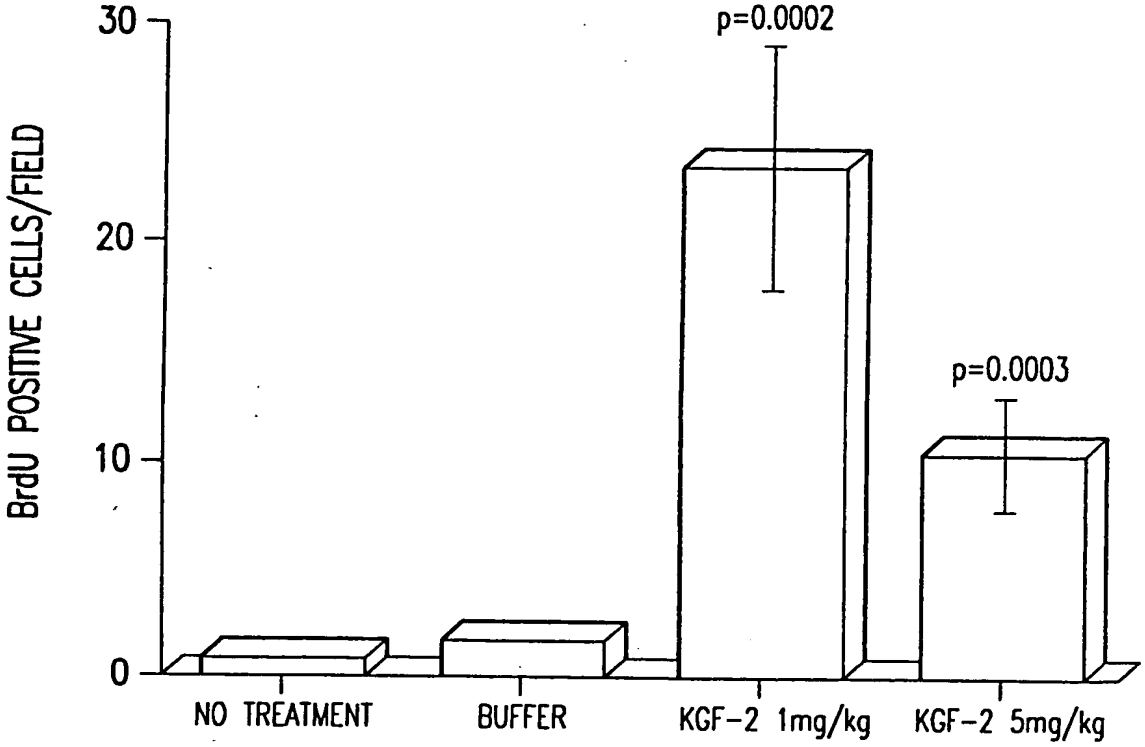

30
20
10
0
BrdU POSITIVE CELLS/FIELD
p=0.0002
p=0.0003
NO TREATMENT
BUFFER
KGF-2 1mg/kg
KGF-2 5mg/kg

FIG. 60

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